UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

IN RE APPLIED THERAPEUTICS SECURITIES LITIGATION	Case No. 1:24-cv-09715 (DLC) (VF) **CLASS ACTION** **JURY TRIAL DEMANDED**

CONSOLIDATED AMENDED CLASS ACTION COMPLAINT

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Lead Plaintiff Dr. Martin Dietrich ("Plaintiff"), individually and on behalf of all others similarly situated, brings this Amended Class Action Complaint (the "Complaint") against Applied Therapeutics, Inc. ("Applied" or the "Company"), Shoshana Shendelman, Ph.D., and Riccardo Perfetti, M.D., Ph.D. (collectively, "Defendants"). Plaintiff's allegations are based upon personal knowledge as to his own actions, and upon information and belief as to all other matters derived from a comprehensive investigation by Plaintiff's counsel. This investigation included an analysis of public filings made by the Company with the United States Securities and Exchange Commission ("SEC"); press releases issued by the Company; presentations conducted by the Company or its executives, officers, or directors; media reports and securities analysts' reports concerning the Company; U.S. Food and Drug Administration ("FDA") reports and information about or concerning the Company; market data regarding the price and trading volume of Applied securities; and other publicly available information. Plaintiff believes additional substantial evidentiary support will be revealed through discovery.

NATURE OF THE ACTION

1. Plaintiff, by and through undersigned counsel, brings this federal securities class action pursuant to Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 (the "Exchange Act"), 15 U.S.C. §§ 78j(b) and 78t(a), and SEC Rule 10b-5 promulgated thereunder, 17 C.F.R. § 240.10b-5, on behalf of all persons and entities that purchased or otherwise acquired the publicly traded common stock of Applied on a U.S. based exchange between January 3, 2024 and December 2, 2024, inclusive (the "Class Period"), and who were damaged thereby (the "Class").

2. Applied is a clinical-stage biopharmaceutical company. During the Class Period, the Company's lead drug candidate, govorestat (also known as AT-007), was in development for the treatment of Classic Galactosemia, a rare pediatric metabolic disorder for which there is no FDA-approved therapy. On the first day of the Class Period, the Company announced that it had

submitted to the FDA a New Drug Application for govorestat to treat Classic Galactosemia (the "NDA"), alongside a Marketing Authorization Application ("MAA") to the European Medicines Agency ("EMA").

3. Undisclosed to investors during the Class Period, the NDA was materially deficient. Between March and June 2021, as part of Applied's ACTION-Galactosemia Kids pediatric galactosemia study (the "Pediatric Study"), 19 of the 47 subjects enrolled at a clinical site—over 40% of the study population—received only approximately 80% of the intended dose of govorestat due to a labeling error (the "Dosing Errors"). The Defendants became aware of the Dosing Errors no later than June 17, 2021, when Applied notified clinical sites of the Dosing Errors, and it distributed corrected materials by June 29, 2021.

4. FDA regulations required the NDA to include a description and analysis of the Dosing Errors and the clinical data recorded from patients who received the Dosing Errors (the "Dosing Errors Clinical Data"). 21 C.F.R. § 314.50(d)(5)(iv).

5. Dr. Shendelman and Dr. Perfetti were instrumental to the Pediatric Study. According to the published results of the Pediatric Study, they both "designed the [Pediatric Study] and interpreted the data," as well as co-authored the results. At the time of the Pediatric Study and the NDA submission, govorestat was Applied's lead drug candidate, and the NDA (and associated application for regulatory approval in Europe) was the first and only application for regulatory approval of one of Applied's drug candidates. Dr. Shendelman and Dr. Perfetti were also instrumental to the "research, development and commercialization objectives" of Applied. They were therefore aware of, or recklessly indifferent to, the clinical results of the Pediatric Study, including the Dosing Errors and the Dosing Errors Clinical Data.

6. Defendants were also familiar with the FDA's regulatory requirements for the NDA. For example, Defendants publicly referenced the significant requirements for approval of a new drug application, including FDA inspections. Also, by Shendelman's own admission at a May 14, 2024 investor conference, Applied "[met] very collaboratively with the FDA prior to submitting our NDA. And we asked them very openly if the data we had generated was acceptable for a potential submission and approval. We wouldn't have submitted otherwise if their answer was no."

7. Defendants therefore were not only familiar with the Dosing Errors and the Dosing Errors Clinical Data, but also that the Dosing Errors and the Dosing Errors Clinical Data were required to be included in the NDA. The omission of the Dosing Errors and the Dosing Errors Clinical Data was therefore either knowing, or severely reckless.

8. However, according to a November 27, 2024 Warning Letter sent by the FDA to Dr. Shendelman (the "Warning Letter"), Applied "failed to provide [the] FDA with any description or analysis of the information describing the nature and extend of the [Dosing Errors]" in the NDA, and instead "reported dose levels for subjects as stated in the protocol…rather than the actual dose levels administered."

9. Nevertheless, the Defendants repeatedly referenced the filing of and acceptance of the NDA, publicized Applied's progress toward regulatory approval, and expressed confidence in the strength of the NDA and that the NDA would be approved. Defendants also repeatedly informed the market that they were preparing to commercialize govorestat. These and other statements alleged herein were materially false and misleading in violation of Section 10(b) and Rule 10b-5 because, among other reasons, the Defendants knew of the Dosing Errors, that the NDA lacked any information about the Dosing Errors and the Dosing Errors Clinical Data, that

the NDA was subject to an FDA inspection where the Dosing Errors would likely be discovered, and that these facts constituted a significant and material risk that the FDA would not approve the NDA.

10. In addition, and also undisclosed to investors during the Class Period, on March 27, 2024, one of Applied's vendors deleted electronic data collected and maintained in an electronic data capture system for critical electronic clinical outcome assessments ("eCOAs") for all 47 subjects in the Pediatric Study (the "Study Data Deletion").

11. Between April 23, 2024 and May 3, 2024, the FDA conducted inspections of at least one Applied clinical testing site. During this inspection, and at an earlier inspection, the FDA was unable to review the deleted data, and thus discovered the Study Data Deletion. During the inspection, the FDA also discovered the Dosing Errors and that the NDA did not contain any information about the Dosing Errors or the Dosing Errors Clinical Data.

12. On May 3, 2024, the FDA gave Dr. Shendelman an Form FDA 483 (the "Form 483"), which is used by the FDA to document "objectional conditions" discovered during an inspection, and discussed the "significant findings" of the Form 483 with Dr. Shendelman. The Form 483 informed Shendelman and Applied of the Study Data Deletion for 11 clinical subjects, specifically that "source [**redacted**] data were entered directly into [the electronic data capture system] for 11 subjects" and Applied's "service provider deleted the source data from [the electronic data capture system] on 03/27/2024 and this data could not be verified."[1] The Form 483 also identified two other objectionable conditions, including data discrepancies between source and generated data and failure to properly document clinical rating changes.

[1] Certain text in the public versions of FDA documents, including the Warning Letter and the Form 483 are redacted by the FDA. The FDA used the term "**(b)(4)**" to indicate redacted material, which has been substituted with the term "[**redacted**]" for easier reading in this Complaint.

13. On May 9, 2023, according to the Warning Letter, Applied responded to the Form 483 and informed the FDA that "source data for 11 subjects, which was captured in [the electronic data capture system] could not be recovered in electronic format."

14. FDA regulations (21 C.F.R. § 312.58) require sponsors of clinical trials, such as Applied, to, upon request from the FDA, permit the FDA to have access to and copy and verify any records and reports relating to a clinical trial. The Study Data Deletion and the permanent loss of the source data for 11 subjects in the Pediatric Study violated these FDA regulations and were a significant negative regulatory event for the chances of the NDA's approval. In fact, the FDA stated in the Warning Letter that the Study Data Deletion affected the FDA's ability to trust the rest of the data supplied by Applied in the NDA. According to the Warning Letter, the FDA was

> concerned that electronic data collected for critical eCOAs was deleted and cannot be verified, which raises concerns about the validity and integrity of the data collected during the clinical investigation. Without access to the pertinent electronic data…including associated audit trails, FDA cannot verify the accuracy, consistency, and completeness of study data collected for critical eCOAs used to measure primary and secondary efficacy endpoints, and cannot evaluate the extent and impact of any reported data errors and discrepancies.

15. Further, the combination of the lack of information about the Dosing Errors and the Dosing Errors Clinical Data in the NDA and the Study Data Deletion "raise[d] significant concerns [for the FDA] about the validity and reliability of data collected" for the NDA.

16. After May 9, 2024, even though the Defendants were aware of the Study Data Deletion and the Form 483, and it was apparent that Applied had violated FDA regulations, Defendants repeatedly made positive representations about the NDA and Defendants' interactions with the FDA concerning the NDA, stating "things are going very well with the FDA," "we don't think that there are any sticking points" or "big issues," communications with the FDA were "very positive and sort of normal course," and "we're very confident in the [NDA approval] process" (May 14, 2024); "we do feel the [NDA] review is going well," "we see an approval in galactosemia

in the near term," and there had been "additional derisking" concerning NDA approval (September 10, 2024); and "overall our message there is that things are going well. We're very encourage by the dialogue with the FDA," and that Applied was "in a good place to successfully launch" govorestat (November 12, 2023).

17. Defendants also provided post-May 9, 2024 regulatory updates concerning the NDA. On May 9, 2024, when discussing a previously announced extension of the FDA's deadline to issue a decision on the NDA, the Defendants stated that "[n]o additional data or studies have been requested by the FDA at this time."

18. Also, on August 7, 2024, Defendants announced that:

> in the process of preparing for FDA inspection, it was discovered that the vendor we engaged to compile NIH Toolbox data for the Company used an adult formula for calculation of about one third of composite cognition and motor skills scores. Adjusting the formula to the pediatric formula resulted in significantly improved data for cognition as compared to the prior data, demonstrating improvement in the govorestat treated group….

19. Then, on September 18, 2024, Defendants disclosed that the FDA had cancelled the upcoming anticipated Advisory Committee meeting to discuss the NDA and govorestat, which Dr. Shendelman stated was "positive news" at an industry conference later that day.

20. These regulatory updates concerned issues separate and apart from the failure to include information about the Dosing Errors and Dosing Errors Clinical Data in the NDA or the Study Data Deletion.

21. These and other statements by the Defendants alleged herein were materially false and misleading in violation of Section 10(b) and Rule 10b-5 because, among other reasons, once Defendants chose to speak about the status of FDA interactions and provide other positive regulatory updates, especially updates that occurred as a result of an FDA inspection, they were required to disclose all known material information concerning those topics, including the Form

483, the Study Data Deletion, the inability to recover electronic source data for 11 subjects, and that the NDA failed to include information about the Dosing Errors or the Dosing Errors Clinical Data. The failure to disclose this information led the market to believe that there were only positive developments, that approval of the NDA was a formality, and that there were no material negative factors that could lead the FDA to reject the NDA.

22. Defendants' materially false and misleading statements artificially inflated the price of Applied common stock during the Class Period. The price of Applied Common Stock increased from a closing price on January 2, 2024, immediately before the start of the Class Period, of $3.64 per share, to a closing price on November 27, 2024, immediately before the Defendants announced the FDA had rejected the NDA of $8.57 per share, and reached a Class Period high price of $10.624 per share on November 11, 2024.

23. Also, on the strength of these misrepresentation, the Defendants sold securities during the Class Period. Dr. Shendelman sold a total of 1,157,382 shares of her Applied common stock for total proceeds of $6,696,111.64, profiting from the Company's artificially inflated share price. The majority of these sales were concentrated over just three days, from August 12 to 14, 2024, when Dr. Shendelman sold 777,014 shares of her Applied common stock at an average price of $6.06 per share for total proceeds of $4,712,048.77. This was just a few days after Defendants provided a regulatory update on August 7, 2024. Moreover, on March 1, 2024, during the Class Period, the Company completed a $100 million private placement of 12,285,714 shares of common stock (at the purchase price of $7.00 per share) and 2,000,000 pre-funded warrants to purchase common stock.

24. The truth began to emerge on Wednesday November 27, 2024, when, during post-market hours the evening before Thanksgiving, the Company issued a press release disclosing that

it had received a Complete Response Letter (the "CRL") from the FDA, and that "the CRL indicates that the FDA completed its review of the [NDA] and determined that it is unable to approve the NDA in its current form, citing deficiencies in the clinical application." Defendants however did not disclose the receipt of Warning Letter at this time, which Dr. Shendelman received that day.

25. In response, on Friday November 29, 2024 (the next trading day after the Thanksgiving Holiday), the price of Applied common stock declined $6.54 per share, or 76.3%, from a closing price of $8.57 per share on November 27, 2024 to a closing price of $2.03 per share on November 29, 2024, on extremely high volume.

26. Applied's common stock continued its decline on Monday December 2, 2024, closing at $1.75 per share, a decline of $0.28 per share, on very high volume. Then, during post-market hours on December 2, 2024, the Company filed a Form 8-K with the SEC, and finally disclosed that it had received the Warning Letter.

27. On December 3, 2024, during market hours, the FDA posted a copy of the Warning Letter, which disclosed that the Company's NDA violated the FDA regulations by failing to include information about the Dosing Errors and the Dosing Errors Clinical Data, the Study Data Deletion, and that these issues raised serious concerns about, among other things, "the validity and reliability of date collected for this clinical investigation." On December 4, 2024, several news outlets reported on the FDA's findings, further disseminating the news to the market. In response to these disclosures, the price of Applied common stock fell $0.37 per share, or 21.1%, over a two-day period, from a closing price on Monday December 2, 2024 of $1.75 per share to a closing price on Wednesday December 4, 2024 of $1.38 per share, on above average volume.

28. Then, on Friday December 5, 2024, Stat News published an article titled "Why Applied Therapeutics has a credibility problem," stating, among other things that Dr. Shendelman "repeatedly misled investors prior to the Food and Drug Administration's rejection of the company's rare-disease drug." In response, the price of Applied common stock fell $0.09 per share, or 6.5%, from a closing price on December 4, 2024 of $1.38 per share, to a closing price on December 5, 2024 of $1.29 per share, on above average volume.

29. These disclosures sharply contradicted Defendants' repeated assurances during the Class Period that there were, for example, no "major sticking points" or "big issues" in the NDA process and that interactions with the FDA were "very positive." In truth, Defendants had concealed critical information that went to the core of govorestat's approvability and misled investors as to the NDA's true prospects.

30. Finally, on December 20, 2024, during pre-market hours, the Company issued a press release and filed a Form 8-K with the SEC announcing that on December 19, 2024, Dr. Shendelman had stepped down from her roles as President, CEO, Secretary, and Chair. In response, the price of Applied common stock fell an additional $0.14 per share, or 13.7%, from a closing price of $1.02 per share on December 19, 2024 to a closing price of $0.88 per share on December 20, 2024, on above average volume.

31. As a result of Defendants' materially false and misleading statements and omissions, investors suffered significant losses when the true facts were disclosed to the market. In the few weeks between the first disclosure of the CRL and the rejection of the NDA on November 27, 2024, to Dr. Shendelman's announced departure on December 20, 2024, Applied's common stock plummeted $7.69 per share, or 89.7%, from $8.57 per share to $0.88 per share.

JURISDICTION AND VENUE

32. This Court has subject matter jurisdiction over this action pursuant to Section 27 of the Exchange Act, 15 U.S.C. § 78aa, and 28 U.S.C. § 1331, because this action arises under the laws of the United States, specifically Sections 10(b) and 20(a) of the Exchange Act and SEC Rule 10b-5.

33. Venue is proper in this District pursuant to Section 27 of the Exchange Act, 15 U.S.C. § 78aa, and 28 U.S.C. § 1391(b), because Applied maintains its principal executive offices in this District, and many of the acts and omissions giving rise to the claims alleged herein, including the preparation, issuance, and dissemination of materially false and misleading statements, occurred within this District.

34. In connection with the acts, conduct, and other wrongs alleged in this Amended Complaint, Defendants, directly or indirectly, used the means and instrumentalities of interstate commerce, including, but not limited to, the U.S. mails, interstate telephone communications, and facilities of national securities exchanges.

PARTIES

A. Lead Plaintiff

35. Lead Plaintiff Dr. Martin Dietrich, as set forth in his certification previously filed as ECF No. 27-2 in connection with his Motion for Appointment as Lead Plaintiff, and which is incorporated herein by reference, purchased shares of Applied common stock during the Class Period at artificially inflated prices and suffered out-of-pocket damages of more than $388,000 related to the Defendants' alleged materially false and misleading statements.

B. Defendants

36. Defendant Applied Therapeutics, Inc. is a Delaware corporation with its principal executive offices located at 545 Fifth Avenue, Suite 1400, New York, New York 10017. Applied

is a clinical-stage biopharmaceutical company engaged in the development of drug candidates targeting rare diseases. During the Class Period, Applied's common stock was publicly traded on the Nasdaq Global Select Market under the ticker symbol "APLT."

37. Defendant Shoshana Shendelman, Ph.D., is the founder of Applied and served throughout the Class Period as the Company's Chief Executive Officer ("CEO"), President, Secretary, and Chair of the Board of the Directors ("Board"). Dr. Shendelman received her B.S. in biochemistry from Brandeis University and a Ph.D. in Cellular, Molecular and Biophysical Studies from Columbia University. As the Company's highest-ranking executive, Dr. Shendelman exercised substantial control over Applied's operations and communications with investors. She personally made or authorized many of the materially false and misleading statements alleged herein and certified the Company's public filings with the SEC. Dr. Shendelman resigned from her positions as CEO, President, Secretary, and Chair of the Board on December 19, 2024, shortly after the CRL and Warning Letter were received by Applied and disclosed by Applied and the FDA.

38. Defendant Riccardo Perfetti, M.D., Ph.D. was, at all relevant times, Applied's Chief Medical Officer ("CMO"). As CMO, Dr. Perfetti was responsible for overseeing the Company's clinical development activities and regulatory strategy. Dr. Perfetti received his M.D. and Ph.D. in Endocrinology from University La Sapienza in Rome, Italy and received post-graduate training in endocrinology and molecular biology at the U.S. National Institutes of Health ("NIH"). During the Class Period, Dr. Perfetti made or had authority over multiple public statements concerning the clinical trial results of the Pediatric Study, and the contents and status of the Company's NDA for govorestat, including statements alleged herein to have been materially false and misleading.

39. Defendants Dr. Shendelman and Dr. Perfetti (collectively, the "Individual Defendants"), because of their respective positions at Applied, possessed the power and authority to control the contents of the Company's SEC filings, press releases, and investor communications. Each was provided with or had access to copies of the Company's public statements alleged herein to be false and misleading before, or shortly after, they were issued. Each had the ability and opportunity to prevent the issuance of such statements or cause them to be corrected. By virtue of their positions and access to material non-public information, the Individual Defendants knew or recklessly disregarded that the adverse facts specified herein had not been disclosed to, and were being concealed from, investors, and that the positive representations they made or caused to be made were materially false and misleading.

40. Applied is liable for the acts of the Individual Defendants and its other employees and agents under the doctrine of *respondeat superior* and common law principles of agency, as all the wrongful conduct alleged herein was undertaken within the scope of their employment and with the Company's authorization. The scienter of the Individual Defendants and other Company agents is imputed to Applied under applicable law.

SUBSTANTIVE ALLEGATIONS

A. The Defendants' Fraudulent Conduct and Materially False and Misleading Statements

1. Background on Govorestat and Classic Galactosemia

41. Govorestat is a novel, orally-administered aldose reductase inhibitor ("ARI") designed to penetrate the central nervous system and treat Classic Galactosemia, a rare, inherited metabolic disorder that predominantly affects children and can be life-threatening if left untreated.

42. Galactosemia is a caused by a genetic defect that renders patients unable to metabolize galactose, a simple sugar. In healthy individuals, galactose is broken down by a series of enzymes. However, in individuals with Classic Galactosemia, one of these key enzymes,

galactose-1-phosphate uridylyltransferase, is either defective or absent. As a result, galactose and its byproducts, particularly galactitol, accumulate in the blood and tissues, causing toxicity.

43. The buildup of galactitol is especially harmful and can result in severe neurological complications, including deficiencies in speech, cognition, motor function, and behavior. As of the Class Period, there were no FDA-approved treatments for Classic Galactosemia. The only available intervention was dietary restriction of galactose, which provides only partial benefit and does not prevent long-term neurological damage.

44. Applied developed govorestat to reduce levels of galactitol in both the blood and brain. The Company claimed that by lowering galactitol, govorestat could provide tangible clinical benefits, such as improved cognitive performance, enhanced motor skills, and better behavioral outcomes. Because no other therapies existed, investor perception of Applied's value was closely tied to the successful development and regulatory approval of govorestat.

45. According to Applied's Annual Report on Form 10-K for the fiscal year ended December 31, 2023, filed with the SEC on March 6, 2024 (the "2023 Form 10-K"), at 5, the Company did "not have any product candidates approved for sale and ha[s] not generated any revenue." Therefore, if the NDA was approved, govorestat would be the first product that Applied would make commercially available.

2. The Clinical Trials that Supported the NDA

46. Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined. In Phase 1, the drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an initial indication of its effectiveness. In Phase 2, the drug typically is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific

targeted diseases and to determine dosage tolerance and optimal dosage. In Phase 3, the drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the safety and efficacy of the product for approval, to establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.

47. In advance of clinical testing, an applicant (such as Applied) is required to agree with the FDA to a protocol that includes dosing, with the understanding that the protocol will be sufficiently statistically powered to indicate whether the drug is safe and effective. For example, as stated in Applied's 2023 Form 10-K (at 27):

> Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the [Investigational New Drug Application (IND)].

48. The Company's first clinical trial targeting Classic Galactosemia was the ACTION-Galactosemia Phase 1/2 Study of adults, initiated in June 2019 (the "Adult Study"). In that trial, Applied measured galactitol levels in both plasma and the brain (using MRI quantitation) to assess the drug's pharmacodynamic impact.

49. Applied's 2023 Form 10-K (at 12) described the Adult Study as follows:

> ACTION-Galactosemia Phase 1/2 Study
>
> We have evaluated AT-007 in a pivotal Phase 1/2 clinical trial in healthy volunteers and adults with Galactosemia. The Phase 1 portion of the study in healthy volunteers evaluated safety, tolerability, CNS penetrance and PK of AT-007 at doses of 5mg/kg to 40mg/kg for up to seven days of consecutive treatment. The Phase 2 portion in adults with Galactosemia evaluated safety, tolerability, PK and pharmacodynamic reduction in the biomarker galactitol. Patients received AT-007 5mg/kg, 20mg/kg, 40mg/kg or placebo, for 28 days.
>
> AT-007 treatment resulted in a statistically significant and robust reduction in plasma galactitol versus placebo in adult Galactosemia patients. Reductions in galactitol were dose dependent, with higher concentrations of AT-007 resulting in

> a greater magnitude of reduction in galactitol. At the higher doses tested (20mg/kg and 40mg/kg), AT-007 significantly reduced plasma galactitol by approximately 50% from baseline. Results were statistically significant (p value of less than 0.01) vs. placebo. Galactitol reduction was rapid and sustained over time. No substantial change from baseline was observed in placebo treated patients. AT-007 was well tolerated in both Galactosemia patients and healthy volunteers.

50. On July 10, 2024, the results of the Adult Study were published in *The Journal of Clinical Pharmacology* in an article titled "Safety, Pharmacokinetics, and Pharmacodynamics of the New Aldose Reductase Inhibitor Govorestat (AT-007) After a Single and Multiple Doses in Participants in a Phase 1/2 Study" (the "7/10/2024 Adult Study Results").

51. The authors of the 7/10/2024 Adult Study Results were Dr. Shendelman; Dr. Perfetti; Evan Bailey, M.D., who, during the Class Period, was Applied's Vice President Clinical Development and medical lead for Galactosemia; Stella Wang, MPH, MS; Richard Mills, PhD; and Ramon Mohanlal, MD, PhD, MBA. Dr. Perfetti was listed as the "corresponding author" of the 7/10/2024 Adult Study Results.

52. According to the 7/10/2024 Adult Study Results' Conflict of Interest disclosure (at 9), "Riccardo Perfetti, Evan Bailey, Stella Wang, and Shoshana Shendelman, are employees and shareholders of Applied Therapeutics Inc. [and] Ramon Mohanlal, is a consultant for Applied Therapeutics."

53. Further, according to the 7/10/2024 Adult Study Results (at 9):

> Riccardo Perfetti, Evan Bailey, Stella Wang, and Shoshana Shendelman designed and performed the study and analyzed the data respectively. Richard Mills, performed the pharmacokinetic and modeling analyses. Ramon Mohanlal, analyzed the data and wrote the manuscript. All authors critically reviewed the manuscript and approved the final version for publication.

54. On June 15, 2020, Applied announced the launch of its Pediatric Study (the ACTION-Galactosemia Kids Study, also referred to as ACTION-Kids or AT-007-1002).

55. Applied's 2023 Form 10-K (at 12) described the Pediatric Study as follows:

ACTION-Galactosemia Kids

In June 2020, we initiated the ACTION-Galactosemia Kids pediatric Galactosemia study. The study was placed on partial clinical hold in August 2020 while we worked with the FDA to redesign and operationally modify the study to seamless design to ensure continuous treatment and the opportunity to receive clinical benefit. The study re-started in February 2021 and was unblinded in April 2023, and patients who were randomized to active treatment transitioned to an expanded access program. The open-label extension for patients that were initially randomized to placebo is ongoing. The pediatric clinical trial was a 2-part study to evaluate safety, pharmacokinetics, and reduction in the toxic biomarker, galactitol (Part A), as well as impact on functional outcomes in children with Galactosemia over time (Part B). Three age cohorts were studied in parallel: age 2-6, age 7-12, and age 13-17. The biomarker portion of the study, demonstrated a 40% reduction in plasma galactitol ($p<0.001$ vs. placebo). The clinical outcomes portion of the study measured several aspects of the Galactosemia phenotype on how patients feel and function. AT-007 treatment demonstrated consistent long-term clinical outcomes benefit across a range of functional measures in the ACTION-Galactosemia Kids trial, and improved activities of daily living, behavior, cognition, fine motor skills, adaptive skills and tremor vs. placebo. The primary endpoint, the Global Statistical Test, was a composite sum of change comprised of four endpoints: OWLS-2 Oral Expression (OE), OWLS-2 Listening Comprehension (LC), BASC-3 Behavior Symptoms Index (BSI) and the BASC-3 Activities of Daily Living (ADL). An additional pre-specified sensitivity analysis included cognition in the primary endpoint (NIH-Toolbox Cognition Battery). Additional clinical outcomes were assessed as secondary endpoints, including adaptive skills and tremor. Clinical outcomes were assessed every 6 months by a firewalled independent Data Monitoring Committee (DMC). While statistical significance defined as a p value of <0.05 was not met on the primary endpoint, systematic improvement over time was demonstrated for the overall primary endpoint ($p=0.1030$) and for a pre-specified sensitivity analyses including cognition ($p=0.0698$). Speech and language components of the primary endpoint were not impacted, which is suspected to be due to lack of progression in the placebo group and concomitant speech therapy received in the trial. Of note, patients with severe speech deficits showed a favorable trend towards improvement with AT-007 treatment vs. placebo. AT-007 (govorestat) provided a statistically significant benefit on tremor at 18 months ($p=0.0428$), as measured by the Archimedes Spiral Drawing Test, and adaptive skills as assessed by the BASC-3 Adaptive Skills Index ($p=0.0265$). Consistent with prior reported data, improvement in galactitol levels was sustained throughout the trial with no impact on Gal-1p or galactose, further establishing the causal role of galactitol in disease pathogenesis. AT-007 continued to be safe and well-tolerated in all age groups; there were no treatment-related serious adverse events (SAEs) reported.

56. On November 6, 2024, the results from the Pediatric Study were published in the *Journal of Clinical Pharmacology* in an article titled "Results of the ACTION-Galactosemia Kids

Study to Evaluate the Effects of Govorestat in Pediatric Patients with Classic Galactosemia" (the "11/6/2024 Pediatric Study Results").

57. The 11/6/2024 Pediatric Study Results had been submitted for publication on October 15, 2024 and accepted for publication on November 6, 2024.

58. The authors of the 11/6/2024 Pediatric Study Results included Dr. Shendelman, Dr. Perfetti, Dr. Bailey, Stella Wang, and others. Dr. Perfetti was listed as the corresponding author. Dr. Shendelman, Dr. Perfetti, Dr. Bailey, and Stella Wang were employees and shareholders of Applied at the time the Article was published.

59. According to the 11/6/2024 Pediatric Study Results, Dr. Shendelman, Dr. Perfetti, Dr. Bailey, Stella Wang "designed the study and interpreted the data," Dr. Perfetti and Dr. Bailey "wrote the manuscript," and [a]ll authors critically reviewed the manuscript and approved the final version for publication."

60. The 11/6/2024 Article did not mention the Study Data Deletion, the Dosing Errors, or the Dosing Errors Clinical Data.

3. Applied Submitted the NDA to the FDA in December 2023, But the NDA Omitted FDA Required Information About the Dosing Errors and the Dosing Errors Clinical Data

61. Assuming successful completion of the required clinical testing, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of a new drug application requesting approval to market the product for one or more indications.

62. According to the 2023 Form 10-K, in December 2023, Applied submitted a new drug application for govorestat for the treatment of Classic Galactosemia (the NDA) to the FDA.

63. As stated by the FDA in the Warning Letter (at 3):

> In order to permit FDA to make a knowledgeable judgment about a new drug application, **FDA regulations require applicants for new drug applications to provide FDA with a description and analysis of any data or information relevant to an evaluation of the safety and effectiveness of the drug product obtained or otherwise received by the applicant from any source, including information derived from clinical investigations**. [(emphasis added).]

64. 21 C.F.R. § 314.50 is titled "Content and Format of an NDA." 21 C.F.R. § 314.50(d)(5)(iv), titled "Technical sections," states, in relevant part:

> (d) Technical Sections. The NDA is required to contain the technical sections described below. Each technical section is required to contain data and information in sufficient detail to permit the agency to make a knowledgeable judgment about whether to approve the NDA or whether grounds exist under section 505(d) of the Federal Food, Drug, and Cosmetic Act to refuse to approve the NDA. The required technical sections are as follows:…
>
> (5) Clinical data section. **A section describing the clinical investigations of the drug, including the following**:…
>
> (iv) **A description and analysis of any other data or information relevant to an evaluation of the safety and effectiveness of the drug product obtained or otherwise received by the applicant from any source, foreign or domestic, including information derived from clinical investigations, including controlled and uncontrolled studies of uses of the drug other than those proposed in the NDA**, commercial marketing experience, reports in the scientific literature, and unpublished scientific papers. [(emphasis added).]

65. Between March and June 2021, Applied supplied clinical sites for the Pediatric Study with mislabeled doses of govorestat. As a result, at least 19 subjects of the 47 subjects, or 40% of the clinical subjects, received 80% of the protocol required dose. As stated in the Warning Letter (at 3-4):

> Specifically, according to Applied Therapeutics' October 19, 2023, Clinical Study Report for Protocol [**redacted**] which was submitted to [the] FDA on December 28, 2023, the [**redacted**] was provided by [**redacted**] as a [**redacted**] mg/mL.
>
> However, during [the] FDA's inspection of Site [**redacted**] FDA found that [**redacted**] had supplied the clinical sites for Protocol [**redacted**] with [**redacted**] mislabeled as [**redacted**] mg/mL, when in fact the amount of [**redacted**] supplied by [**redacted**] was [**redacted**] mg/mL. As a result of this error, **between March and June 2021, clinical sites administered 80% of the protocol-required dose to subjects. Specifically, at least 19 subjects** [**redacted**] **received a lower dosage**

> **of** [**redacted**] **[govorestat] than the protocol required**. On June 17, 2021, Applied Therapeutics notified clinical sites of this error, and on June 29, 2021, clinical sites were provided with a new formulation of [**redacted**] [govorestat] at the correct concentration [**redacted**] mg/mL. Clinical sites were also provided with an updated version of the pharmacy manual, with instructions on drug administration. [(emphasis added).]

66. However, Applied did not disclose the Dosing Errors or report the Dosing Errors Clinical Data in the NDA, and instead reported clinical results as if the correct protocol required dose had been administered. As stated by the FDA in the Warning Letter (at 4):

> Applied Therapeutics **failed to provide FDA with any description or analysis of the information describing the nature and extent of the dosing errors related to the mislabeled** [**redacted**]. Specifically, Applied Therapeutics **reported dose levels for subjects as stated in the protocol (for example,** [**redacted**] **mg/kg), rather than the actual dose levels administered**. [(emphasis added).]

67. The failure to inform the FDA about the Dosing Errors or report the Dosing Errors Clinical Data was a violation of FDA requirements and regulations, including 21 C.F.R. § 314.50(d)(5)(iv), because **"[i]nformation on the nature and extent of the dosing errors is relevant to an evaluation of the safety and effectiveness of the investigational drug product.**" Warning Letter at 4 (emphasis added).

> Therefore, Applied Therapeutics **failed to provide sufficient information at the time of submission of the application to enable FDA to make an informed decision regarding the impact of the dosing-error incident on study data**. This failure **raises significant concerns about the validity, reliability, and integrity of the data for Protocol** [**redacted**]. Furthermore, Applied Therapeutics' failure to disclose this critical information **raises significant concerns about the sponsor's oversight and conduct of clinical investigations, including its compliance with the reporting requirements for human drug products**. [Warning Letter at 4 (emphasis added).]

68. During the Class Period, Applied did not disclose the Dosing Errors, the Dosing Errors Clinical Data, that the NDA failed to include either the Dosing Errors or the Dosing Errors Clinical Data, or that the NDA failed to comply with FDA regulations.

69. As alleged herein, Dr. Shendelman and Dr. Perfetti designed the Pediatric Study, reviewed the resulting data, and authored the 11/6/2024 Pediatric Study Results. During and before the Class Period, when the NDA was prepared and submitted, govorestat was the Company's lead drug candidate, and govorestat to treat Classic Galactosemia was the first indication the Company was seeking to commercialize. According to the 2023 Form 10-K (at 73), Applied was also "highly dependent" on Dr. Shendelman and Dr. Perfetti, and "the loss of the services of either of [them] could impede the achievement of [Applied's] research, development and commercialization objectives."

70. As the persons who designed the Pediatric Study of the Company's lead drug candidate, and key employees of Applied, Dr. Shendelman and Dr. Perfetti would have had actual knowledge of or were deliberately reckless in failing to know about any deviation in the protocol for the Pediatric Study, such as the Dosing Errors and the Dosing Errors Clinical Data.

71. It also was not until March 19, 2025, months after the end of the Class Period and start of this litigation that Applied hired a Chief Regulatory Officer to serve as part of the Company's executive leadership team and be responsible for leading the Company's global regulatory strategy. Therefore, during the Class Period, Dr. Shendelman, as CEO, President, Secretary, Chair, and a key employee, and Dr. Perfetti, as CMO and a key employee, were responsible for the oversight of regulatory affairs and strategy, including the submission of the all-critical NDA and communications with the FDA.

72. There is therefore a strong inference that, at the time the NDA was prepared and submitted to the FDA, Dr. Shendelman and Dr. Perfetti were aware of the NDA for govorestat, the contents of the NDA, including the lack of information concerning the Dosing Errors and Dosing

Errors Clinical Data in the NDA, and were also responsible to ensure that the NDA complied with all FDA regulations.

73. At the start of, and throughout, the Class Period, Defendants also knew that the FDA's approval process for the NDA was rigorous, and that the NDA was required to include all clinical data for govorestat, including the data related to the Dosing Errors. As stated in Applied's 2023 Form 10-K (at 27), which was signed by Dr. Shendelman:

> In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. **Failure to comply with the applicable United States requirements at any time during the drug development process, approval process or after approval, may subject an applicant to delays and a variety of administrative or judicial sanctions, such as the FDA's refusal to approve a pending New Drug Application, or NDA, withdrawal of an approval, imposition of a clinical hold, issuance of warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.**
>
> **The process required by the FDA before a drug may be marketed** in the United States generally involves:…
>
> - submission to the FDA of an NDA for marketing approval, which must include data from preclinical testing and clinical trials;
> - satisfactory completion of an FDA advisory committee review, if applicable;
> - satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with [current good manufacturing practice ("cGMP")] requirements, and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
> - **satisfactory completion of an FDA inspection of selected clinical sites to assure compliance with [Good Clinical Practices ("GCPs")] and the integrity of the clinical data**;…
> - FDA review and approval of the NDA. [(emphasis added).]

74. Also, as admitted by Dr. Shendelman on May 14, 2024, Dr. Shendelman and Applied met "very collaboratively with the FDA prior to submitting our NDA. And we asked them very openly if the data we had generated was acceptable for a potential submission and approval. We wouldn't have submitted otherwise if their answer was no." At a minimum, it would have been extremely reckless not to confirm whether the Dosing Errors and Dosing Errors Clinical Data was required to be included in the NDA as part of these "very collaborative" discussions about "acceptable" data for the NDA.

75. Based upon these facts, there is a strong inference that Dr. Shendelman and Dr. Perfetti, and through them Applied, knew, or were severely reckless in not knowing, (a) of the Dosing Errors and the Dosing Errors Clinical Data, (b) of the FDA's regulatory requirements for the content of the NDA, (c) that information on the nature and extent of the Dosing Errors and Dosing Errors Clinical Data was relevant to the FDA's evaluation of the safety and effectiveness of govorestat, and (d) that information concerning the Dosing Errors and the Dosing Errors Clinical Data had to be included in the NDA.

76. Further, it would have been, at a minimum, extremely reckless not to include all clinical data for the Pediatric Study, including the Dosing Errors and Dosing Errors Clinical Data, in the NDA when the Defendants knew the FDA would conduct a pre-approval inspection in which the Dosing Errors would almost certainly be discovered, which would present a substantial risk to approval. In fact, the FDA did discover the Dosing Errors and the lack of information about the Dosing Errors and Dosing Errors Clinical Data in the NDA through an inspection of Applied's clinical sites from April 27, 2024 and May 3, 2024.

4. Defendants Made Materially False and Misleading Statements Concerning the Clinical Data Underlying and Supporting the NDA

a) Defendants' January 3, 2024 Press Release and Form 8-K Concerning Filing the NDA Contained Materially False and Misleading Statements

77. On January 3, 2024, the first day of the Class Period, during pre-market hours, the Company issued a press release titled "Applied Therapeutics Announces MAA Validation and NDA Submission of Govorestat (AT-007) for Treatment of Classic Galactosemia" (the "1/3/2024 Press Release"). Also on January 3, 2024, during pre-market hours, the Company filed a Form 8-K with the SEC (the "1/3/2024 Form 8-K"). The 1/3/2024 Form 8-K was signed by Dr. Shendelman and contained some of the same information in the 1/3/2024 Press Release.

78. The 1/3/2024 Press Release and 1/3/2024 Form 8-K both separately stated:

> *{FS1}*[2] **The NDA and MAA submission packages include clinical outcomes data from the Phase 3 registrational ACTION-Galactosemia Kids study in children age[d] 2-17 with Galactosemia, the Phase 1/2 ACTION-Galactosemia study in adult patients with Galactosemia, and preclinical data**. The FDA has a 60-day filing review period to determine whether the NDA is complete and accepted for review.

79. Dr. Shendelman was quoted in the 1/3/2024 Press Release stating *{FS2}* **"We look forward to working closely with both regulatory agencies throughout the review process and hope to bring the first treatment to patients with Galactosemia soon.**"

80. FS1 and FS2 were materially false and misleading in violation of Section 10(b) and Rule 10b-5 because they contained untrue statements of material fact or omitted to state material facts necessary in order to make the statements made not misleading. Specifically, at the time these statements were made, Dr. Shendelman and Applied were aware of, or were severely reckless in not knowing, that (a) FDA regulations required the NDA to include "a description and analysis of

[2] The statements Lead Plaintiff alleges are false and misleading are bolded and underlined and prefaced with "*{FS_}*" for numbering purposes.

any other data or information relevant to an evaluation of the safety and effectiveness of [govorestat] obtained or otherwise received by [Applied] from any source…including information derived from clinical investigations," (b) that the Dosing Errors and Dosing Errors Clinical Data was such "other data or information," (c) that in the NDA, Applied failed to provide the FDA with a description or analysis of the Dosing Errors or the Dosing Errors Clinical Data, and (d) that instead, as the FDA subsequently stated, Applied "reported dose levels for subjects as stated in the protocol…rather than the actual dose levels administered."

81. By failing to disclose these material facts, Dr. Shendelman and Applied misled investors and the public, who as a result, reasonably believed that (a) the NDA complied with FDA regulations, (b) the NDA contained all required information and clinical results from the Pediatric Study, (c) the NDA accurately reported the clinical data Applied obtained for the study, and (d) there were no known material risks to approval of the NDA, when in fact this was not true.

82. Further, Defendants knew, or recklessly disregarded, that they would be subject to an FDA investigation in connection with the NDA, and as such there was a significant risk that the Dosing Errors and Dosing Errors Clinical Data would be discovered by the FDA. As such, these undisclosed facts were negative material factors and a significant risk that the FDA would not approve the NDA because they raised significant concerns about the validity, reliability, and integrity of the clinical data and Applied's oversight and conduct of its clinical investigations. As such, Dr. Shendelman and Applied did not have a reasonable basis to speak concerning the likelihood of approval of the NDA, and once they chose to speak concerning the NDA and the likelihood of NDA approval, had a duty to disclose all material facts concerning those subjects to ensure that a reasonable investor would not be misled.

83. The same day, analysts from UBS Global Research and Evidence Lab issued a report that reacted positively to the announcement that the NDA had been submitted, and noted that the "key events expected over the next 12 months included govorestat (AT-007) galactosemia NDA acceptance" which was understood to be "expected 1Q24."

84. On February 22, 2024, analyst Leerink Partners initiated coverage of Applied with a recommendation of outperform and a price target of $12 per share.

b) Defendants' February 28, 2024 Press Releases and February 29, 2024 Form 8-K Concerning the FDA's Acceptance of the NDA and Applied's $100 Million Private Placement Contained Materially False and Misleading Statements Concerning the NDA and Commercialization of Govorestat

85. On February 28, 2024, during pre-market hours, the Company issued a press release titled "Applied Therapeutics Announces FDA Acceptance and Priority Review of New Drug Application for Govorestat for the Treatment of Classic Galactosemia" (the "2/28/2024 NDA Press Release"), which announced that the FDA had (a) accepted its NDA, (b) granted Priority Review status (a fast track designation), (c) assigned a Prescription Drug User Fee Act ("PDUFA") target action date of August 28, 2024, and (d) noted that it was planning to hold an advisory committee meeting to discuss the NDA.

86. PDUFA is a statute that, among other things, established a timeline for review of new drug applications, generally ten months for most applications and six months for those with priority review.

87. Also on February 28, 2024, during pre-market hours, the Company issued a press release titled "Applied Therapeutics Announces $100 Million Private Placement" (the "2/28/2024 Placement Press Release"), that announced a $100 million private placement of common stock and pre-funded warrants that was scheduled to close on March 1, 2024 (the "3/1/2024 Private Placement"):

> The Company entered into a definitive securities purchase agreement, dated as of February 27, 2024, for the sale of 12,285,714 shares of the Company's common stock, par value $0.0001 per share at a purchase price of $7.00 per share (the "Shares") and 2,000,000 pre-funded warrants to purchase common stock at a purchase price of $6.999, which is equal to the purchase price per share of common stock less the $0.001 per share exercise price of each pre-funded warrant (the "Pre-Funded Warrants" and together with the Shares, the "Securities"), in a private placement (the "Private Placement"). The Private Placement is expected to result in gross proceeds to the Company of approximately $100 million, before deducting placement agent commissions and other offering expenses.
>
> The financing consisted of participation from new and existing investors, including Perceptive Advisors, Janus Henderson Investors, Venrock Healthcare Capital Partners, Adage Capital Partners, Frazier Life Sciences, Logos Capital, Vestal Point Capital, and Rock Springs Capital.
>
> The Private Placement is expected to close on or about March 1, 2024, subject to the satisfaction of customary closing conditions.

88. On February 29, 2024, during post-market hours, the Company filed a Form 8-K with the SEC (the 2/29/2024 Form 8-K"). The 2/29/2024 Form 8-K was signed by Dr. Shendelman, disclosed again the information in the 2/28/2024 NDA Press Release and 2/28/2024 Placement Press Release, and attached as an exhibit the 2/28/2024 Placement Press Release.

89. The 2/28/2024 NDA Press Release and the 2/29/2024 Form 8-K both separately made a statement substantially similar to FS1, which was false and misleading for the same reasons as FS1 as stated in paragraphs 80-82:

> *{FS3}* **The [NDA] submission package included clinical outcomes data from the Phase 3 registrational ACTION-Galactosemia Kids study in children aged 2-17 with Galactosemia, the Phase 1/2 ACTION-Galactosemia study in adult patients with Galactosemia, and preclinical data.**

90. Dr. Shendelman was quoted in the 2/28/2024 NDA Press Release, stating that the FDA's actions were a "critical milestone:"

> *{FS4}* **The FDA's acceptance of the NDA for govorestat for the treatment of Galactosemia represents a critical milestone for Applied Therapeutics and more importantly, for patients with Galactosemia and their families. The Agency's decision to grant Priority Review for this NDA underscores the urgent unmet medical need as there are currently no treatment options for this**

> **devastating disease,**… We want to thank the patients, families, collaborators and physicians involved in reaching this achievement. *{FS5}* **We look forward to continuing to work with the FDA throughout the review process, as we hope to bring govorestat to patients as quickly as possible**.

91. FS4 and FS5 were materially false and misleading in violation of Section 10(b) and Rule 10b-5 because they contained untrue statements of material fact or omitted to state material facts necessary in order to make the statements made not misleading. Specifically, at the time these statements were made, Dr. Shendelman and Applied were aware of, or were severely reckless in not knowing, that (a) FDA regulations required the NDA to include "a description and analysis of any other data or information relevant to an evaluation of the safety and effectiveness of [govorestat] obtained or otherwise received by [Applied] from any source…including information derived from clinical investigations," (b) that the Dosing Errors and Dosing Errors Clinical Data was such "other data or information," (c) that in the NDA, Applied failed to provide the FDA with a description or analysis of the Dosing Errors or the Dosing Errors Clinical Data, and (d) that instead, as the FDA subsequently stated, "reported dose levels for subjects as stated in the protocol…rather than the actual dose levels administered."

92. By failing to disclose these material facts, Dr. Shendelman and Applied misled investors and the public, who as a result, reasonably believed that (a) the NDA complied with FDA regulations, (b) the NDA contained all required information and clinical results from the Pediatric Study, (c) the NDA accurately reported the clinical data Applied obtained for the study, and (d) there were no known material risks to approval of the NDA, when in fact this was not true.

93. Further, Defendants knew, or recklessly disregarded, that they would be subject to an FDA investigation in connection with the NDA, and as such there was a significant risk that the Dosing Errors and Dosing Errors Clinical Data would be discovered by the FDA. As such, these undisclosed facts were negative material factors and a significant risk that the FDA would not

approve the NDA because they raised significant concerns about the validity, reliability, and integrity of the clinical data and Applied's oversight and conduct of its clinical investigations. As such, Dr. Shendelman and Applied did not have a reasonable basis to speak concerning the likelihood of approval of the NDA, and once they chose to speak concerning the NDA and the likelihood of NDA approval, had a duty to disclose all material facts concerning those subjects to ensure that a reasonable investor would not be misled.

94. On February 28, 2024, the price of Applied common stock increased $1.82 per share, or 32.6%, from a closing price on February 27, 2024 of $5.58 per share, to a closing price of $7.40 per share on February 28, 2024, on volume that was more than 13 times the previous day's trading volume.

c) Defendants' March 6, 2024 Press Release, Form 8-K, and Form 10-K Concerning 2023 Financial Results Contained Materially False and Misleading Statements Regarding the NDA and Commercialization of Govorestat

95. On March 6, 2024, during pre-market hours, the Company issued a press release titled "Applied Therapeutics Reports Fourth Quarter and Year-end 2023 Financial Results" (the "3/6/2024 Press Release"). Also during pre-market hours on March 6, 2024, the Company filed a Form 8-K with the SEC that attached the 3/6/2024 Release as an Exhibit (the "3/6/2024 Form 8-K"). The 3/6/2024 Form 8-K was signed by Dr. Shendelman.

96. In addition, on March 6, 2024, during pre-market hours, the Company filed its 2023 Form 10-K, which was signed by Dr. Shendelman and other executives and directors of Applied.

97. The 3/6/2024 Press Release and 2023 Form 10-K both restated FS1, which was false and misleading for the same reasons as FS1, as stated in paragraphs 80-82.

> *{FS1}* **The NDA and MAA submission packages include[d] clinical outcomes data from the Phase 3 registrational ACTION Galactosemia Kids study in children age[d] 2-17 with Galactosemia, the Phase 1/2 ACTION-Galactosemia study in adult patients with Galactosemia, and preclinical data.**

98. The 3/6/2024 Press Release also stated.

> *{FS6}* **The Company intends to use the net proceeds [of the 3/1/2024 Private Placement] to fund commercial activities for govorestat** and to further develop other pipeline candidates, and for working capital and general corporate purposes. With cash of approximately $153.5 million as of March 1, 2024, the Company is well-capitalized with an expected runway into the first half of 2026.

99. Dr. Shendelman was also quoted in the 3/6/2024 Press Release, stating:

> *{FS7}* **We've made significant clinical and regulatory progress, particularly with the NDA acceptance and MAA validation for govorestat for the treatment of Galactosemia, achieving key milestones for our rare disease pipeline.** …
>
> *{FS8}* **As Applied enters into this next stage of growth, we are poised for continued value generation across our rare disease pipeline, supported by our recent financing and bolstered cash position.**

100. FS6 through FS8 were materially false and misleading in violation of Section 10(b) and Rule 10b-5 because they contained untrue statements of material fact or omitted to state material facts necessary in order to make the statements made not misleading. Specifically, at the time these statements were made, Dr. Shendelman and Applied were aware of, or were severely reckless in not knowing, that (a) FDA regulations required the NDA to include "a description and analysis of any other data or information relevant to an evaluation of the safety and effectiveness of [govorestat] obtained or otherwise received by [Applied] from any source…including information derived from clinical investigations," (b) that the Dosing Errors and Dosing Errors Clinical Data was such "other data or information," (c) that in the NDA, Applied failed to provide the FDA with a description or analysis of the Dosing Errors or the Dosing Errors Clinical Data, and (d) that instead, as the FDA subsequently stated, "reported dose levels for subjects as stated in the protocol…rather than the actual dose levels administered."

101. By failing to disclose these material facts, Dr. Shendelman and Applied misled investors and the public, who as a result, reasonably believed that (a) the NDA complied with FDA regulations, (b) the NDA contained all required information and clinical results from the Pediatric

Study, (c) the NDA accurately reported the clinical data Applied obtained for the study, and (d) there were no known material risks to approval of the NDA, when in fact this was not true.

102. Further, Defendants knew, or recklessly disregarded, that they would be subject to an FDA investigation in connection with the NDA, and as such there was a significant risk that the Dosing Errors and Dosing Errors Clinical Data would be discovered by the FDA. As such, these undisclosed facts were negative material factors and a significant risk that the FDA would not approve the NDA because they raised significant concerns about the validity, reliability, and integrity of the clinical data and Applied's oversight and conduct of its clinical investigations. As such, Dr. Shendelman and Applied did not have a reasonable basis to speak concerning the likelihood of approval of the NDA or commercialization of govorestat, and once they chose to speak concerning these topics, had a duty to disclose all material facts concerning those subjects to ensure that a reasonable investor would not be misled.

103. The 2023 Form 10-K (at 45) also included a risk factor that "Our future success is substantially dependent on the successful clinical development, regulatory approval and commercialization of our product candidates. If we are not able to obtain required regulatory approvals, we will not be able to commercialize our product candidates and our ability to generate product revenue will be adversely affected." The 2023 Form 10-K continued, in part:

> Prior to obtaining approval to commercialize any product candidate in the United States or abroad, *{FS9}* **we must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA or comparable foreign regulatory authorities, that such product candidate is safe and effective for its intended uses.** Results from preclinical studies and clinical trials can be interpreted in different ways. Even if we believe that the preclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. The FDA may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or post-approval, or it may object to elements of our clinical development program, requiring their alteration.

104. FS9 was materially false and misleading in violation of Section 10(b) and Rule 10b-5 at the time it was made because it contained untrue statements of material fact or omitted to state material facts necessary in order to make the statements made, in the light of the circumstances under which they were made, not misleading. At the time this statement was made, the risk that Applied may not be able to demonstrate "with substantial evidence" and "to the satisfaction of the FDA" that govorestat "is safe and effective for its intended use" was not a potential future risk. Rather, it had already occurred because the Defendants had submitted the NDA without any mention of the Dosing Errors or the Dosing Errors Clinical Data, which was required "evidence" to prove that govorestat was "safe and effective for its intended use."

105. Attached to the 2023 Form 10-K as Exhibit 31.1 was a signed certification, dated March 6, 2024, by Dr. Shendelman pursuant to the Sarbanes Oxley Act stating:

> I have reviewed this Form 10-K of Applied Therapeutics, Inc.;
>
> *{FS10}* **Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report**.

106. FS10 was materially false and misleading in violation of Section 10(b) and Rule 10b-5 because it was an untrue statement of fact. Dr. Shendelman knew that FS1 and FS9 were included in the 10-K and were materially false and misleading.

107. On March 14, 2024, Dr. Shendelman sold 318,573 shares of Applied common stock at the artificially inflated price of $5.39, for proceeds of $1,717,108.47. This sale amounted to approximately 3.76% of Dr. Shendelman's then-current holdings.

108. Research analysts found Applied's statements about and related to NDA approval to be important and give a positive view of the Company. On March 6, 2024, UBS Securities raised its price target for Applied from $4 per share to $12 per share as the Company was expecting

"continued success." Nine days later, on March 15, 2024, UBS Securities raised the price target again to $13 per share.

109. On March 25, 2024, analyst RBC Capital Markets initiated coverage of Applied with a price target for Applied common stock of $12 per share and a rating of outperform. RBC told investors that Applied was "well-positioned for success" in the orphan disease galactosemia and SORD deficiency and saw "ample room for additional appreciation" in the shares due to a forecast of more than $650 million in aggregate peak revenue. RBC expected continued upside momentum and saw "a favorable setup into/through upcoming regulatory decisions."

d) Applied's March 11, 2024 Investor Presentation Contained Materially False and Misleading Statements Concerning the Pediatric Study Trial Results

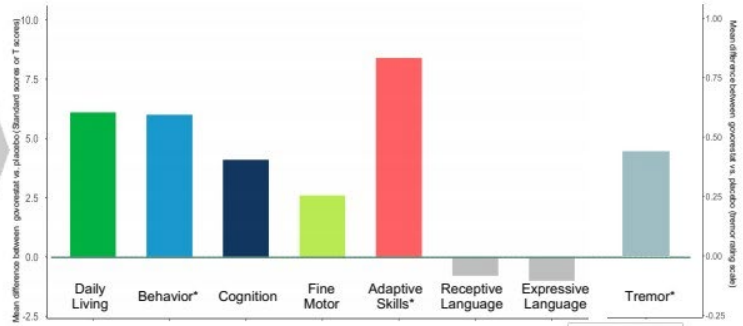
110. On March 11, 2024, during pre-market hours, Applied filed a Form 8-K with the SEC that attached "a presentation that contains company information to be used by members of management from time to time in a series of meetings with analysts, investors and other third parties" (the "3/11/2024 Form 8-K" attaching the "3/11/2024 Investor Presentation"). The 3/11/2024 Form 8-K was signed by Dr. Shendelman

111. *{FS11}* Slides 14-18 of the 3/11/2024 Investor Presentation contained statements regarding the results of the Pediatric Study, including the dosages given and the clinical results achieved:

Govorestat Treatment Reduced Plasma Galactitol Levels by 40% (p<0.001 vs. placebo); Improvement in Galactitol Biomarker Provided Clinical Benefit Across Activities of Daily Living, Behavior, Cognition, Adaptive Skills and Tremor

Weight Group	AT-007 Dose (QD)	% Reduction From Baseline
>40kg	15mg/kg	38.29%
20-40kg	20mg/kg	41.43%
<20kg	30mg/kg	39.83%
All groups	**15-30mg/kg**	**40.19% (p<0.001)**

- Significant improvement in galactitol biomarker vs. placebo
- Sustained over time through 18 months of treatment
- No compensatory increase in galactose or Gal-1p



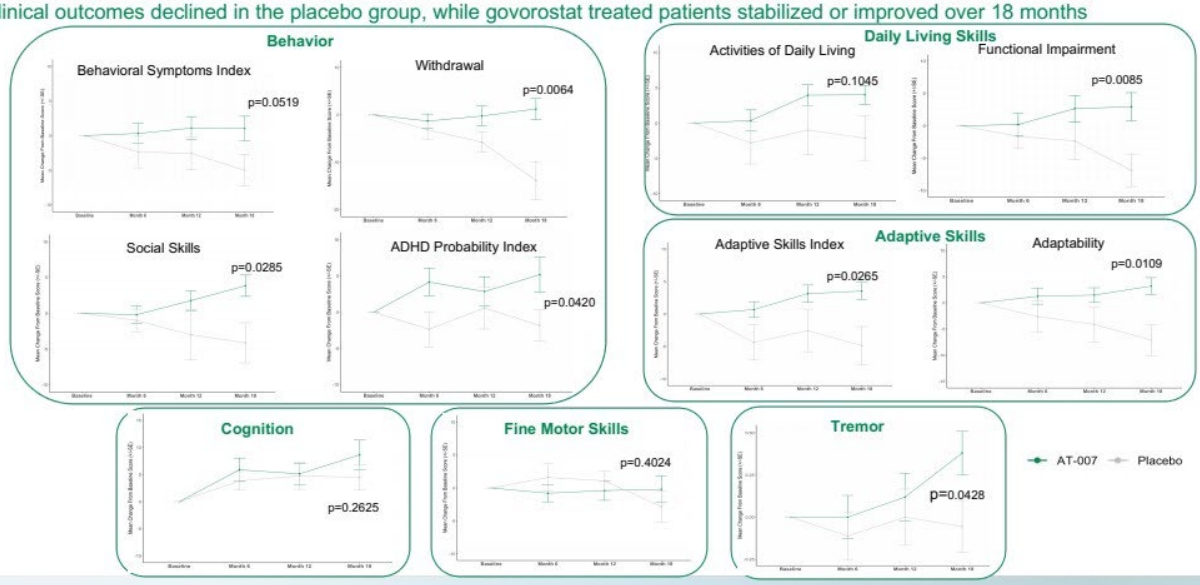
*Several components of the BASC test (prespecified secondary endpoints) demonstrated statistically significant benefit of govorestat treatment vs. placebo at 18 months, including adaptive skills (p=0.0265); adaptability (p=0.0109); withdrawal (p=0.0064), social skills (p=0.0285); ADHD index (p=0.0420); functional impairment (p=0.0085). Tremor (another prespecified secondary endpoint) was also statistically significant at 18 months (p=0.0428).

Speech endpoints were not impacted by govorestat treatment, which is suspected to be due to lack of progression in the placebo group and concomitant speech therapy received by almost all children in the trial. Of note, patients with severe speech deficits showed a favorable trend towards improvement with AT-007 vs. placebo. Tremor is measured on a different scale vs. other tests, and is referenced by the right-hand y axis.

APPLIED THERAPEUTICS 14

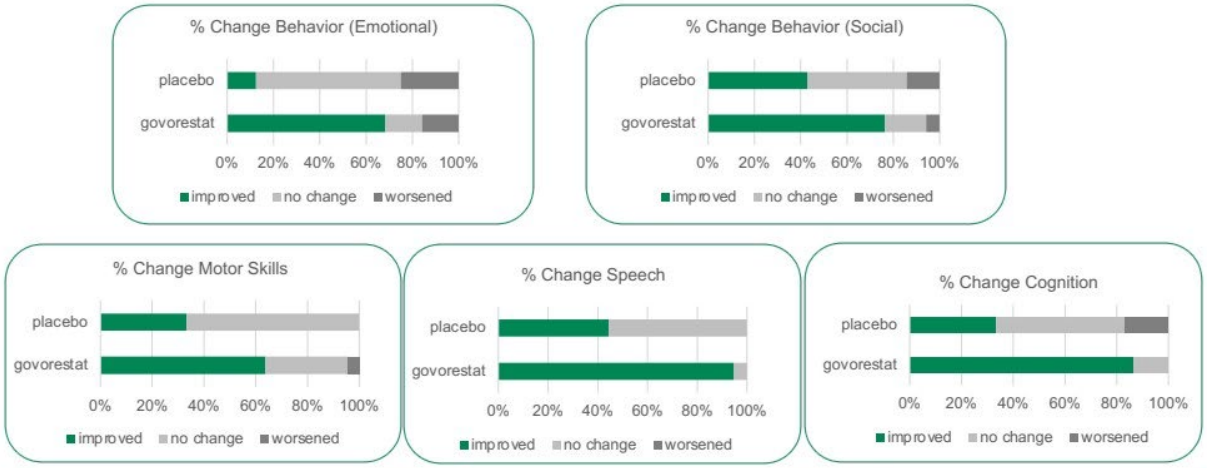
Govorestat Treatment Positively Impacted Behavior, Daily Living Skills, Adaptive Skills, Cognition, Fine Motor Skills & Tremor

Clinical outcomes declined in the placebo group, while govorestat treated patients stabilized or improved over 18 months



APPLIED THERAPEUTICS 15

Caregiver Exit Interviews Support the Clinical Meaningfulness of Govorestat Treatment



Caregivers noted an improvement or stabilization of disease on all categories of symptoms in the govorestat treated group vs. placebo.*

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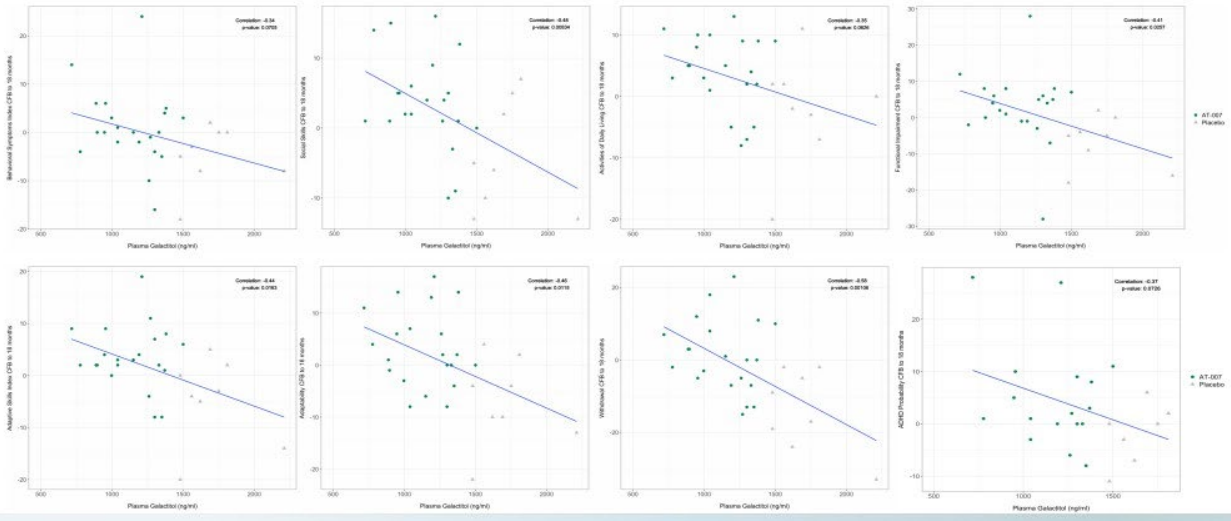
*Exit interviews were performed prior to study unblinding to prevent bias

16

Galactitol Reduction Correlated with Clinical Outcomes Benefit

Galactitol level at 3 months statistically correlated with change in clinical outcomes at 18 months



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CFB= Change From Baseline; correlation plots include data for all subjects who completed the same BASC test at baseline and 18 months (e.g. preschool, child, adolescent)

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Safety Summary

- Govorestat was safe and well-tolerated with no serious adverse events
- All adverse events were mild to moderate
- Adverse events & lab values were balanced between govorestat and placebo groups

	Placebo (N=16) Number (%) of Subjects	Govorestat (N=31) Number (%) of Subjects
Subjects reporting at least one TEAE	16 (100%)	30 (96.8%)
Gastrointestinal disorders	11 (68.8%)	23 (74.2%)
Hepatic enzyme increased	2 (12.5%)	8 (25.8%)
Urine albumin/creatinine ratio increased	7 (43.8%)	5 (16.1%)
Urine protein/creatinine ratio increased	3 (18.8%)	2 (6.5%)
Renal & urinary disorders	1 (6.3%)	3 (9.7%)
Infections and infestations	10 (62.5%)	18 (58.1%)

TEAE= treatment emergent adverse event; Refers to patients having reported at least 1 term in AE category; AE, adverse event

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112. FS11 was materially false and misleading in violation of Section 10(b) and Rule 10b-5 at the time it was made because the slides contained untrue statements of material fact or omitted to state material facts necessary in order to make the statements made, in the light of the circumstances under which they were made, not misleading. Slide 6 of the 3/11/2024 Investor Presentation stated that the NDA had been accepted. At the time the slides were published, Dr. Shendelman and Applied knew that there were additional clinical results for the Pediatric Study that were not disclosed in FS11 or the NDA, namely the Dosing Errors Clinical Data. Reasonable investors would conclude that the results included in the 3/11/2024 Investor Presentation were the same results that were used to support the NDA. By failing to disclose the Dosing Errors or the Dosing Errors Clinical Data, Defendants led investors to believe that the results described above were the complete results of the Pediatric Study, and there were no other results from the study that were required to be included in the NDA.

e) Defendants' March 28, 2024 Press Release Contained Materially False and Misleading Statements Concerning the NDA and Commercialization of Govorestat

113. On March 28, 2024, during post-market hours, the Company issued a press release titled "Applied Therapeutics Provides FDA Update on PDUFA Target Action Date for Govorestat for the Treatment of Classic Galactosemia" (the "3/28/2024 Press Release"). The 3/28/2024 Press Release announced that the FDA had extended the review period for its NDA for govorestat by three months, setting a new PDUFA target action date of November 28, 2024. Defendants reassured analysts and investors that the FDA's request for additional time to review the NDA was part of the FDA's "routine information requests."

114. On March 29, 2024, during post-market hours, the Company issued a Form 8-K that disclosed again the extension of the PDUFA target action date for the NDA by three months (the "3/29/2024 Form 8-K"). The 3/29/2024 Form 8-K was signed by Dr. Shendelman.

115. The 3/28/2024 Press Release and 3/29/2024 Form 8-K both separately restated FS3, a statement substantially similar to FS1, which was false and misleading for the same reasons as FS1 as stated in paragraphs 80-82:

> *{FS3}* **The [NDA] submission package included clinical outcomes data from the Phase 3 registrational ACTION-Galactosemia Kids study in children aged 2-17 with Galactosemia, the Phase 1/2 ACTION-Galactosemia study in adult patients with Galactosemia, and preclinical data.**

116. Dr. Shendelman was also quoted in the 3/28/2024 Press Release as stating:

> *{FS12}* **While the PDUFA action date extension represents a delay, we remain confident in the potential for govorestat approval for Galactosemia and we will continue to work closely with the FDA throughout the review process**.

117. FS12 was materially false and misleading in violation of Section 10(b) and Rule 10b-5 because it contained untrue statements of material fact or omitted to state material facts necessary in order to make the statements made not misleading. Specifically, at the time these

statements were made, Dr. Shendelman and Applied were aware of, or were severely reckless in not knowing, that (a) FDA regulations required the NDA to include "a description and analysis of any other data or information relevant to an evaluation of the safety and effectiveness of [govorestat] obtained or otherwise received by [Applied] from any source…including information derived from clinical investigations," (b) that the Dosing Errors and Dosing Errors Clinical Data was such "other data or information," (c) that in the NDA, Applied failed to provide the FDA with a description or analysis of the Dosing Errors or the Dosing Errors Clinical Data, and (d) that instead, as the FDA subsequently stated, "reported dose levels for subjects as stated in the protocol…rather than the actual dose levels administered."

118. By failing to disclose these material facts, Dr. Shendelman and Applied misled investors and the public, who as a result, reasonably believed that (a) the NDA complied with FDA regulations, (b) the NDA contained all required information and clinical results from the Pediatric Study, (c) the NDA accurately reported the clinical data Applied obtained for the study, and (d) there were no known material risks to approval of the NDA, when in fact this was not true.

119. Further, Defendants knew, or recklessly disregarded, that they would be subject to an FDA investigation in connection with the NDA, and as such there was a significant risk that the Dosing Errors and Dosing Errors Clinical Data would be discovered by the FDA. As such, these undisclosed facts were negative material factors and a significant risk that the FDA would not approve the NDA because they raised significant concerns about the validity, reliability, and integrity of the clinical data and Applied's oversight and conduct of its clinical investigations. As such, Dr. Shendelman and Applied did not have a reasonable basis to speak concerning the likelihood of approval of the NDA, and once they chose to speak concerning the NDA and the

likelihood of NDA approval, had a duty to disclose all material facts concerning those subjects to ensure that a reasonable investor would not be misled.

120. Also on March 28, 2024, UBS reported that, based on its call with Dr. Shendelman, "FDA did not request new data," and emphasized that the extension "has nothing to do with carcinogenicity or QT studies." Applied told UBS that the carcinogenicity study was still ongoing and that the QT study had been completed "with no QT prolongation observed." Applied management also confirmed to UBS that an Advisory Committee ("AdComm") meeting was still expected later in 2024, with the likely focus to be on "safety, surrogacy of galactitol levels, and clinical meaningfulness of govorestat's efficacy." UBS characterized the delay as potentially "an incremental negative," but nonetheless stated that it continued to view approval as "likely" based on the Company's reassurances, and that Applied was "aiming for full approval across all ages."

> PDUFA now 11/28/2024 - FDA needs additional time to review suppl. Analyses FDA has extended the review period for the govorestat (AT-007) NDA in galactosemia by 3 months - new PDUFA 11/28/2024. APLT provided supplemental analyses (of existing data) in response to "FDA's routine information requests" (specific details not provided), which were considered a "Major Amendment to the NDA" and thus additional time (3mos) is required to review the information. The knee jerk reaction is that this could be an incremental negative but, following our conversation with mgmt (not related to carcinogenicity or QT data - see below), we continue to see approval as likely. Regarding the AdComm (likely 3Q24, in our view), we expect safety, surrogacy of galactitol levels, and clinical meaningfulness of govorestat's efficacy to be the focal points.
>
> Takeaways from mgmt f/u call - more analyses need more time to review We caught up with mgmt (CEO Shoshana Shendelman) - key takeaways include:
>
> 1) FDA did not request new data - the timeline extension is purely based on additional analyses of existing data. FDA has been requesting information since the NDA submission (specific requests not disclosed). This PDUFA extension has nothing to do with carcinogenicity or QT studies - the carcinogenicity study is ongoing (data not ready yet), while the QT study has completed with no QT prolongation observed (APLT will discuss the potential QT data submission with FDA at the mid-cycle meeting).

> 2) AdComm still expected - the schedule is currently unknown - APLT expects to get more information during the mid-cycle meeting with FDA (likely in May), and will then communicate to the Street.
>
> 3) No changes in FDA division composition - there have been no changes of note to the review team/division.
>
> 4) Aiming for full approval across ages - post-market study in adults is likely required.

121. On April 12, 2024, RBC Capital Markets reiterated its outperform rating and $12 per share price target for Applied common stock.

f) Defendants' April 15, 2024 Press Release Announcing a New Chief Commercial Officer Contained Materially False and Misleading Statements Concerning the Commercialization of Govorestat

122. On April 15, 2024, during pre-market hours, the Company issued a press release titled "Applied Therapeutics Appoints Dale Hooks as Chief Commercial Officer" (the "4/15/2024 Press Release"). The 4/15/2024 Press Release announced the appointment of Dale Hooks as Applied's new Chief Commercial Officer. Dr. Shendelman was quoted in the 4/15/2025 Press Release as stating:

> I am pleased to welcome Dale to Applied, *{FS13}* **particularly at this critical stage in the company's lifecycle as we approach the govorestat potential approval and launch**…
>
> *{FS14}* **As we move towards becoming a commercial stage organization, we are committed to building out a strong and credentialed leadership team with experience launching rare disease therapies. I believe that Dale's breadth of experience in commercial leadership roles and proven track record with product launches will be invaluable in bringing Applied from a development company to a commercial organization.**

123. FS13 and FS14 were materially false and misleading in violation of Section 10(b) and Rule 10b-5 because they contained untrue statements of material fact or omitted to state material facts necessary in order to make the statements made not misleading. Specifically, at the time these statements were made, Dr. Shendelman and Applied were aware of, or were severely

reckless in not knowing, that (a) FDA regulations required the NDA to include "a description and analysis of any other data or information relevant to an evaluation of the safety and effectiveness of [govorestat] obtained or otherwise received by [Applied] from any source…including information derived from clinical investigations," (b) that the Dosing Errors and Dosing Errors Clinical Data was such "other data or information," (c) that in the NDA, Applied failed to provide the FDA with a description or analysis of the Dosing Errors or the Dosing Errors Clinical Data, and (d) that instead, as the FDA subsequently stated, "reported dose levels for subjects as stated in the protocol…rather than the actual dose levels administered."

124. By failing to disclose these material facts, Dr. Shendelman and Applied misled investors and the public, who as a result, reasonably believed that (a) the NDA complied with FDA regulations, (b) the NDA contained all required information and clinical results from the Pediatric Study, (c) the NDA accurately reported the clinical data Applied obtained for the study, and (d) there were no known material risks to approval of the NDA, when in fact this was not true.

125. Further, Defendants knew, or recklessly disregarded, that they would be subject to an FDA investigation in connection with the NDA, and as such there was a significant risk that the Dosing Errors and Dosing Errors Clinical Data would be discovered by the FDA. As such, these undisclosed facts were negative material factors and a significant risk that the FDA would not approve the NDA because they raised significant concerns about the validity, reliability, and integrity of the clinical data and Applied's oversight and conduct of its clinical investigations. As such, Dr. Shendelman and Applied did not have a reasonable basis to speak concerning the likelihood of approval of the NDA or upcoming commercialization of govorestat, and once they chose to speak concerning these topics, had a duty to disclose all material facts concerning those subjects to ensure that a reasonable investor would not be misled.

126. On April 22, 2024 during post-market hours, the Company re-filed the 2023 Form 10-K as an Annual Report to Security Holders with the SEC. As such, Defendants Applied and Dr. Shendelman restated FS1, FS9, and FS10 in the 2023 Form 10-K on April 22, 2024.

5. The FDA Conducted an Inspection, and on May 3, 2024, Informed Applied of the Study Data Deletion Through the Form 483 and Discussions with Dr. Shendelman

127. On March 25, 2024, the FDA pre-announced an inspection of one of Applied's clinical testing sites. This clinical testing site was involved in the Pediatric Study. Warning Letter at 2.

128. In the Pediatric Study, Applied "used Pearson's Q-global®, a Web-based administration system for capturing data for certain electronic clinical outcome assessments [eCOAs] performed for measuring primary and secondary efficacy endpoints." Warning Letter at 2.

129. On March 27, 2024 the Study Data Deletion occurred and Applied's vendor deleted electronic data in Q-global® for all 47 subjects in the Pediatric Study:

> [A] third-party vendor contracted by Applied Therapeutics deleted electronic data in Q-global®, including associated audit trails, for the [**redacted**] for all 47 subjects enrolled in the study at all [**redacted**] clinical sites. As a result, during the sponsor inspection, FDA was unable to access and copy and verify records and reports relating to the study conducted under Protocol [**redacted**] specifically certain electronic data collected and maintained in Q-global® for critical eCOAs for all 47subjects at multiple study timepoints for this clinical investigation. [Warning Letter at 2.]

130. Between Monday April 29, 2024 and Friday May 3, 2024, the FDA conducted the inspection that was pre-announced on March 25, 2024. "This inspection was conducted as a part of FDA's Bioresearch Monitoring [("BIMO")] Program, which includes inspections designed to evaluate the conduct of research and to help ensure that the rights, safety, and welfare of human subjects have been protected." Warning Letter at 1.

131. The BIMO inspection program is designed to ensure the integrity of data submitted in NDAs and to verify that clinical trials are conducted in accordance with applicable federal regulations, including Good Clinical Practices (GCPs) standards and subject protection requirements.

132. As described by the Warning Letter (at 2), "FDA regulations require sponsors, upon request from an authorized officer or employee of the FDA, at reasonable times, to permit such an officer or employee to have access to and copy and verify any records and reports relating to a clinical investigation."

133. 21 C.F.R. § 312.58(a), titled "Inspection of sponsor's records and reports – FDA inspection" provides that:

> FDA inspection. A sponsor shall upon request from any properly authorized officer or employee of the Food and Drug Administration, at reasonable times, permit such officer or employee to have access to and copy and verify any records and reports relating to a clinical investigation conducted under this part. Upon written request by FDA, the sponsor shall submit the records or reports (or copies of them) to FDA. The sponsor shall discontinue shipments of the drug to any investigator who has failed to maintain or make available records or reports of the investigation as required by this part.

134. "Applied Therapeutics failed to adhere to these requirements." Warning Letter at 2. During the inspection and an earlier inspection of another clinical site, the "FDA requested access to verify electronic data collected and maintained in Q-global®." Warning Letter at 2. However, because of the Study Data Deletion, "during the [the FDA's] sponsor inspection, FDA was unable to access and copy and verify records and reports relating to the [Pediatric Study] specifically certain electronic data collected and maintained in Q-global® for critical eCOAs for all 47 subjects at multiple study timepoints for this clinical investigation." Warning Letter at 2.

135. At the conclusion of the FDA's inspection on May 3, 2024, the FDA investigators gave the Form 483 to Dr. Shendelman and discussed with her its "significant findings." Warning Letter at 2.

136. The Form FDA 483 was dated May 3, 2024, and addressed to Dr. Shendelman at Applied's New York, NY offices.

137. The Form 483 was prepared and signed by Kerun Haredo, an FDA Investigator, Benton Ketron, an FDA Investigator, and Cheryl Grandinetti, an FDA Center Employee.

138. The Form 483 reported a "Failure to ensure the study is conducted in accordance with the protocol and/or investigation plan" for the Pediatric Study. Specifically, the Form 483 identified:

> 1. Section 11 of the **Clinical Data Validation Plan states that all raw data and electronic data obtained from the Record Forms and publisher-provided software programs will be stored and archived**. Source [**redacted**] data were entered directly into Q-Global Portal by subject parent/caregiver **for 11 subjects at Site** [**redacted**]. **Your service provided deleted the source data from the Q-Global Portal on 03/27/2024 and this data could not be verified.**
>
> 2. Section 10.2 of the Clinical Validation Plan states that quality assurance (QA) procedures will be performed to ensure errors are detected and corrected before final database lock and include re-review of data transferred. **For the collected efficacy endpoint assessments, discrepancies between the source and generated datasets were discovered after the submission of the SDTM [Study Data Tabulation Model] datasets to [FDA] as follows**:

Assessment Name	**Number of Discrepancies**	**Number of Raw Data Items**	**Error Rate**
Oral And Written Language Skills, Second Edition (OWLS-II)	628	39,542	1.6%
National Institute of Health (NIH) 9-Hole Pegboard Dexterity Test	29	170	17%
NIH Cognition Battery Test	58	162	36%
Archimedes Spiral Drawing Test	16	632	2.5%
[Redacted]	468	28,683	1.6%

> [**redacted**] Standard Operating procedure WI-016 Version 2, dated 10/31/2020, section 6.3.1 Data Change Form (DCF) states that a Rating Change Form is used if an assessment was reviewed by a [**redacted**] clinical data reviewer who has

> suggested one of more score of value changes based on the review. This form is to be signed by the original Rater or Principal Investigator authorizing the change. [**redacted**] should not make any updates in the Web Portal until a completed DCF is received from the site. **For approximately 128 rater score change queries, a signed Rating Change Form was not utilized/completed**. [(emphasis added).]

139. Because Dr. Perfetti was the CMO and a key employee of Applied, and also designed the Pediatric Study, there is a strong inference that the issues and protocol deviations identified in the Form 483 would also have been shared with Dr. Perfetti by either the FDA or Dr. Shendelman.

140. According to the FDA website page[3] titled "FDA Form 483 Frequently Asked Questions," a Form 483 is issued "to firm management at the conclusion of an inspection when an investigator(s) has observed any conditions that in their judgment may constitute violations of the Food Drug and Cosmetic (FD&C) Act and related Acts;" "each observation noted on the FDA Form 483 is clear, specific and significant;" a Form 483 "notifies the company's management of objectionable conditions;" and "Form 483s are discussed with a company's management at the conclusion of the inspection. Each observation is read and discussed so that there is a full understanding of what the observations are and what they mean."

> Q: When is an FDA Form 483 issued?
>
> A: An FDA Form 483 is issued to firm management at the conclusion of an inspection **when an investigator(s) has observed any conditions that in their judgment may constitute violations of the Food Drug and Cosmetic (FD&C) Act and related Acts**. FDA investigators are trained to ensure that each observation noted on the FDA Form 483 is clear, specific and significant. Observations are made when in the investigator's judgment, conditions or practices observed would indicate that any food, drug, device or cosmetic has been adulterated or is being prepared, packed, or held under conditions whereby it may become adulterated or rendered injurious to health.

[3] https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-references/fda-form-483-frequently-asked-questions, archived at https://perma.cc/Y5GU-AHZM.

> Q: What is the purpose of an FDA Form 483?
>
> A: The FDA Form 483 **notifies the company's management of objectionable conditions. At the conclusion of an inspection, the FDA Form 483 is presented and discussed with the company's senior management**. Companies are encouraged to respond to the FDA Form 483 in writing with their corrective action plan and then implement that corrective action plan expeditiously.
>
> Q: Is the FDA Form 483 intended to be an all-inclusive list of every possible deviation from law and regulation?
>
> A: No, it's not. The FDA Form 483 is a report which does not include observations of questionable or unknown significance at the time of the inspection. There may be other objectionable conditions that exist at the firm that are not cited on the FDA Form 483. FDA investigators are instructed to note only what they saw during the course of the inspection. Companies are responsible to take corrective action to address the cited objectionable conditions and any related non-cited objectionable conditions that might exist.
>
> Q: How is the FDA Form 483 shared with the company?
>
> A: **FDA Form 483s are discussed with a company's management at the conclusion of the inspection. Each observation is read and discussed so that there is a full understanding of what the observations are and what they mean**.
>
> Q: What are the implications of the FDA Form 483 for agency enforcement and what happens next?
>
> A: The FDA Form 483 does not constitute a final Agency determination of whether any condition is in violation of the FD&C Act or any of its relevant regulations. The FDA Form 483 is considered, along with a written report called an Establishment Inspection Report, all evidence or documentation collected on-site, and any responses made by the company. The Agency considers all of this information and then determines what further action, if any, is appropriate to protect public health. [(emphasis added).]

141. On May 9, 2024, the Company responded to the Form 483 and informed the FDA that "the deleted [**redacted**] source data for 11 subjects, which was captured directly into Q-global®, ***could not be recovered in electronic format***." Warning Letter at 2 (emphasis added).

142. Applied also assured the FDA that the Company recognized the severity of the situation and that the circumstances of the Study Data Deletion would not be replicated. According

to the Warning Letter (at 2-3), in the May 9, 2024 response, Applied "also indicated that steps have been taken to ensure the integrity of the remaining data."

> For example, you stated that you instructed [**redacted**] (the developers of [**redacted**]) to block any further actions regarding data for this study, such that no further data could be deleted. You also stated that [**redacted**] transferred a copy of the remainder of the electronic dataset to Applied Therapeutics for backups, and the data is now warehoused with both [**redacted**] and Applied Therapeutics. In addition, you performed an assessment of systems to ensure that the third-party vendor did not have the capability to delete data from any other systems.
>
> You further stated in your May 9, 2024, written response that preventive actions will be taken, including but not limited to the following:
>
> 1. For any new trial, Applied Therapeutics will create a data process map that clearly shows the flow and storage of collected data, to ensure that source data is maintained at both the site and at the sponsor.
>
> 2. Original paper source documents will remain at the clinical site, with a PDF copy available at the sponsor.
>
> 3. Electronic data (even if held on third-party systems) will be backed up appropriately and held at the sponsor.
>
> 4. External vendors will not have the ability to delete files from any electronic systems.
>
> 5. Appropriate electronic audit trails will be maintained such that any changes to electronic data will be identifiable and auditable. [Warning Letter at 2-3.]

143. Therefore, by May 9, 2024, Dr. Shendelman and Applied knew, and had confirmed to the FDA, that the "source data for 11 subjects, which was captured directly into Q-global®, could not be recovered in electronic format," and as such were aware, or were severely reckless in disregarding, (a) the existence of the Study Data Deletion; (b) that electronic data collected for critical eCOAs for the Pediatric Study was deleted and could not be verified by the FDA as part of its investigation, which was certain to raise concerns about the validity and integrity of the data collected during the Pediatric Study; (c) that Applied, the NDA, and Pediatric Study were in violation of 21 C.F.R. § 312.58 and the terms of the protocol for the Pediatric Study; (d) that

Applied could not rectify the "objectionable condition" identified by the FDA of the deletion of the electronic clinical data for 11 test subjects; (e) that these facts, in addition to the omission of the Dosing Errors and Dosing Errors Clinical Data from the NDA, caused a serious and material risk that the FDA would reject the NDA; and (f) that there existed a serious and material negative regulatory development for the Company's prospects for NDA approval and ability to commercialize govorestat.

144. The Study Data Deletion was in fact a significant negative issue. According to the Warning Letter (at 3):

> Without access to the pertinent electronic data… including associated audit trails, [the] FDA cannot verify the accuracy, consistency, and completeness of study data collected for critical eCOAs used to measure primary and secondary efficacy endpoints, and cannot evaluate the extent and impact of any reported data errors and discrepancies. FDA also cannot confirm whether the clinical investigation was conducted incompliance with the regulatory responsibilities set forth in 21 CFR 312.

145. Further, the combination of the Study Data Deletion and the failure to provide information concerning the Dosing Errors and the Dosing Errors Clinical Data in the NDA increased the FDA's concerns. According to the Warning Letter (at 4):

> Applied Therapeutics' failure to permit FDA access to verify records and reports related to a clinical investigation, and its failure to provide FDA information relevant to an evaluation of the safety and effectiveness of an [**redacted**] raise significant concerns about the validity and reliability of data collected for this clinical investigation.

146. Despite the gravity of this incident, and Defendants' statements that FDA approval of a new drug application is subject to these inspections, Defendants did not disclose that Applied and Dr. Shendelman had received the Form 483 or the objectionable conditions identified in the Form 483 during the Class Period. Such failure to disclose the Study Data Deletion rendered the following statement made in Applied's 2023 Form 10-K (at 27, and as alleged in full context above at paragraph 73) materially false and misleading in violation of Section 10(b) and Rule 10b-5.

{FS15} **The process required by the FDA before a drug may be marketed in the United States generally involves:…satisfactory completion of an FDA inspection of selected clinical sites to assure compliance with [Good Clinical Practices ("GCPs")] and the integrity of the clinical data**;…

147. FS15 was disseminated on March 6, 2024 with the filing of the 2023 Form 10-K, and restated on April 22, 2024 in Applied Annual Report to Stockholders, before the inspection detailed in the Warning Letter took place. However, it was still in the market and public sphere after May 3, 2024, when Defendants were informed that the FDA had discovered the Study Data Deletion, and on May 9, 2024, when Defendants informed the FDA that data for 11 subjects could not be recovered. Failure to disclose the Form 483 or the Study Data Deletion led the market to believe that any inspection of Applied that the FDA conducted revealed no issues, especially in light of other statements made by Defendants (as alleged below) on or after May 9, 2024 that there were, for example, "no sticking points" with the FDA. Defendants were in possession of material information that rendered this statement false and misleading, and therefore had a duty to correct FS15, which did not occur until the Complete Response Letter and Warning Letter were disclosed.

6. Defendants Made Additional Materially False and Misleading Statements With Knowledge of the Dosing Errors and the Study Data Deletion

a) Defendants' May 9, 2024 Press Release, Form 8-K, and Form 10-Q Concerning Applied's Financial Results for the First Quarter of 2024 Contained Materially False and Misleading Statements About the NDA and the Commercialization of Govorestat

148. On May 9, 2024, the same day as Applied Therapeutic's response to the FDA concerning the From 483, during pre-market hours, the Company issued a press release titled "Applied Therapeutics Reports First Quarter 2024 Financial Results" (the "5/9/2024 Press Release"). Also on May 9, 2024, during pre-market hours, the Company filed a Form 8-K with the SEC that attached a copy of the 5/9/2024 Press Release as an exhibit (the "5/9/2024 Form 8-K"). The 5/9/2024 Form 8-K was signed by Dr. Shendelman.

149. In addition, on May 9, 2024, during pre-market hours, the Company filed its Form 10-Q for the first fiscal quarter of 2024 ended March 31, 2024 with the SEC (the "1Q 2024 Form 10-Q"). The 1Q 2024 Form 10-Q was signed by Dr. Shendelman and Les Funtleyder, Applied's Chief Financial Officer ("CFO").

150. The 5/9/2024 Press Release and 1Q 2024 Form 10-Q (at 29) both separately restated FS1, which was false and misleading for the same reasons as set forth in paragraphs 80-82:

> *{FS1}* **The NDA and MAA submission packages include clinical outcomes data from the Phase 3 registrational ACTION-Galactosemia Kids study in children age[d] 2-17 with Galactosemia, the Phase 1/2 ACTION-Galactosemia study in adult patients with Galactosemia, and preclinical data.**

151. The 5/9/2024 Press Release also stated:

> In March 2024, the Company announced that the U.S. Food and Drug Administration (FDA) has extended the review period for the New Drug Application (NDA) for govorestat (AT-007) for the treatment of Classic Galactosemia to allow more time to review supplemental analyses of previously submitted data that had been provided by Applied in response to the FDA's routine information requests. *{FS16}* **No additional data or studies have been requested by the FDA at this time.** The new PDUFA action date is November 28, 2024**.**

152. FS16 was materially false and misleading in violation of Section 10(b) and Rule 10b-5 at the time it was made because it contained untrue statements of material fact or omitted to state material facts necessary in order to make the statements made, in the light of the circumstances under which they were made, not misleading. At the time this statement was made, the FDA had requested "additional data or studies" related to the NDA, namely information regarding the objectionable conditions outlined in the Form 483, including the deleted source data for 11 Pediatric Study participants that could not be recovered. The Form 483 and inquiries in it were not routine.

153. Further, by providing a regulatory update and giving a reason why the PDUFA date was extended, Defendants had an obligation to disclose all known material regulatory update

information, including the receipt of the Form 483 and the objectionable conditions identified therein.

154. FS16 was also materially false and misleading in violation of Section 10(b) and Rule 10b-5 because Dr. Shendelman and Applied knew at the time, and failed to disclose, that there was additional undisclosed clinical information relevant to the determination of the NDA – namely the Dosing Errors Clinical Data. The failure to disclose this information rendered FS16 materially false and misleading as it led investors to believe that there was no additional data that was required to be included in the NDA. By choosing to speak about additional updated data requested by the FDA, they had an obligation to disclose the other additional data that was necessary for the NDA.

155. The 5/9/2024 Press Release discussed the potential launch and commercialization of govorestat, which would first require the FDA to approve the NDA:

> Financial Results…Cash runway: The Company expects that its cash and cash equivalents will fund the business into 2026. *{FS17}* **Additionally, the sale of the priority review voucher (PRV), which would be granted upon a potential NDA approval of govorestat for the treatment of Galactosemia could substantially extend the Company's cash runway.**

156. The rare pediatric disease priority review voucher ("PRV") program aims to incentivize drug development for rare pediatric diseases. Under this voucher program, a sponsor such as Applied who receives an approval for a drug or biological product for a rare pediatric disease may qualify for a voucher that can be redeemed to receive priority review for a different product. The sponsor may also transfer or sell the voucher to another sponsor.

157. Dr. Shendelman was quoted in the press release as stating *{FS18}* "**Preparations are underway for the potential approval and commercial launch of govorestat for the treatment of Classic Galactosemia in the US and EU, following the significant regulatory progress we have already made in 2024."**

158. FS16 through FS18 were materially false and misleading in violation of Section 10(b) and Rule 10b-5 because they contained untrue statements of material fact or omitted to state material facts necessary in order to make the statements made not misleading. Specifically, at the time these statements were made, Dr. Shendelman and Applied were aware of, or were severely reckless in not knowing, that (a) FDA regulations required the NDA to include "a description and analysis of any other data or information relevant to an evaluation of the safety and effectiveness of [govorestat] obtained or otherwise received by [Applied] from any source…including information derived from clinical investigations," (b) that the Dosing Errors and Dosing Errors Clinical Data was such "other data or information," (c) that in the NDA, Applied failed to provide the FDA with a description or analysis of the Dosing Errors or the Dosing Errors Clinical Data, and (d) that instead, as the FDA subsequently stated, "reported dose levels for subjects as stated in the protocol…rather than the actual dose levels administered."

159. Further, Defendants knew, or recklessly disregarded, that they would be, and in fact had already been, subject to an FDA investigation in connection with the NDA, and as such there was a significant risk that the Dosing Errors and Dosing Errors Clinical Data would be discovered by the FDA. As such, these undisclosed facts were negative material factors and a significant risk that the FDA would not approve the NDA because they raised significant concerns about the validity, reliability, and integrity of the clinical data and Applied's oversight and conduct of its clinical investigations.

160. FS16 through FS18 were also materially false and misleading in violation of Section 10(b) and Rule 10b-5 because, at the time these statements were made, Dr. Shendelman and Applied were aware of, or were severely reckless in not knowing, that (a) Applied had informed the FDA that electronic source data for 11 subjects in the Pediatric Study had been

deleted and not been recovered, (b) as a result, this data could not be verified by the FDA as part of its investigation, which raised concerns about the validity and integrity of the data collected during the Pediatric Study, (c) that Applied, the NDA, and Pediatric Study were in violation of 21 C.F.R. § 312.58 and the terms of the protocol for the Pediatric Study; (d) that Applied could not rectify the "objectionable condition" identified by the FDA of the deletion of the electronic clinical data for 11 test subjects; (e) that these facts, in addition to the omission of the Dosing Errors and Dosing Errors Clinical Data from the NDA, were a serious and material risk that the FDA would reject the NDA; and (f) that there existed a serious and material negative development for the Company's prospects for NDA approval and ability to commercialize govorestat.

161. By failing to disclose these material facts, Dr. Shendelman and Applied misled investors and the public, who as a result, reasonably believed that (a) the NDA complied with FDA regulations, (b) the NDA contained all required information and clinical results from the Pediatric Study, (c) the NDA accurately reported the clinical data Applied obtained for the study, (d) the FDA had not identified, and Defendants were not aware of, any issues with the NDA or the clinical data underlying the NDA, and (e) there were no known material risks to approval of the NDA, when in fact this was not true.

162. For these reasons related to the Dosing Errors and the Study Data Deletion, Dr. Shendelman and Applied did not have a reasonable basis to speak concerning the likelihood of approval of the NDA and commercial launch of govorestat, and once they chose to speak concerning regulatory updates and these topics, had a duty to disclose all material facts concerning those subjects to ensure that a reasonable investor would not be misled.

163. In addition, by referencing the "significant regulatory progress we have already made in 2024" and "potential approval and commercial launch of govorestat" in FS18, Dr.

Shendelman and Applied misled investors into thinking there were no negative developments with the FDA, when in fact the FDA had discovered the Study Data Deletion and informed Dr. Shendelman and Applied about it and its seriousness through the Form 483.

164. The 1Q 2024 Form 10-Q (at 48) also included an identical risk factor to FS9 in the Form 10-K:

> Prior to obtaining approval to commercialize any product candidate in the United States or abroad, *{FS19}* **we must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA or comparable foreign regulatory authorities, that such product candidate is safe and effective for its intended uses.**

165. FS19 was materially false and misleading in violation of Section 10(b) and Rule 10b-5 at the time it was made because it contained untrue statements of material fact or omitted to state material facts necessary in order to make the statements made, in the light of the circumstances under which they were made, not misleading. At the time this statement was made, the risk that Applied may not be able to demonstrate "with substantial evidence" and "to the satisfaction of the FDA" that govorestat "is safe and effective for its intended use" was not a potential future risk. Rather, it had already occurred because the Defendants had submitted the NDA without any mention of the Dosing Errors or the Dosing Errors Clinical Data, which was required "evidence" to prove that govorestat was "safe and effective for its intended use," and the FDA was aware of the Study Data Deletion and that electronic source records for 11 subjects in the Pediatric Study were deleted and not recoverable, which was a material negative impediment to proving that govorestat was "safe and effective for its intended use."

166. Attached to the 1Q 2024 Form 10-Q as Exhibit 31.1 was a signed certification, dated May 9, 2024, by Dr. Shendelman pursuant to the Sarbanes Oxley Act stating:

> I have reviewed this Form 10-Q of Applied Therapeutics, Inc.;

{FS20} **Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report.**

167. FS20 was materially false and misleading in violation of Section 10(b) and Rule 10b-5 because it was an untrue statement of fact. Dr. Shendelman knew that FS1 and FS19 were included in the 1Q 2024 Form 10-Q and were materially false and misleading.

168. In reaction to Defendants' false and misleading statements, the market continued to expect that govorestat's FDA approval was imminent. For instance, UBS Global Research and Evidence Lab issued a report on June 4, 2024, that proclaimed that it was still "bullish on Applied Therapeutics (APLT), with the stock well-positioned to outperform in 2H24. In our recent discussion, APLT mgmt noted that the company has not received any update from the FDA for the scheduling of the govorestat's AdCom[m] (PDUFA: Nov. 28th, 2024)." Moreover, UBS reported that "APLT mgmt expressed confidence around the potential launch of Govorestat at YE'24" and "noted that the Galactosemia community is highly active and engaged in the approval process."

b) Dr. Shendelman Made Materially False and Misleading Statements at the May 14, 2024 RBC Capital Markets Global Healthcare Conference Concerning Interactions with the FDA, and Omitted the Study Data Deletion or Form 483

169. On May 14, 2024, during post-market hours, Dr. Shendelman participated in the 2024 RBC Capital Markets Global Healthcare Conference. A transcript of that conference was prepared and distributed by Bloomberg LP.

170. At the RBC Capital Markets Global Healthcare Conference, Dr. Shendelman was asked by Brian Abrahams of RBC Capital Markets about the current status of the NDA and the Company's communications with the FDA concerning the NDA, responding that "thinks are going

very well with the FDA" and that communications have been "very positive and sort of normal course:"

> Q - Brian Abrahams: Got it. And maybe we can talk a little bit about some of the ongoing work in Galactosemia and SORD Deficiency. And maybe starting on Galactosemia, can you talk about the latest status of the FDA review?
>
> A - Shoshana Shendelman: Yes. *{FS21}* **So, things are going very well with the FDA**. Just to recall the timeline here, we submitted our NDA in December and the NDA was accepted in February with priority review, which gave us an initial PDUFA date of August 28th, which is a very close timeline if you think about all the things that have to happen during that review period. We engaged with the FDA. They did delay the PDUFA by three months, we believe because they needed additional time during the review and the PDUFA date is currently November 28th.
>
> *{FS22}* **In that timeframe though, we have worked very successfully with them**. **We've been having some interesting conversations**. You don't just submit an NDA and then wait for the PDUFA date to come. As you well know, there's a lot of meetings that happen. *{FS23}* **There's a lot of interactions with FDA in the interim and that's all going very well and on track and we feel very encouraged**.
>
> Q - Brian Abrahams: Can you elaborate a little bit more? I guess, was there any sort of one particular area that the FDA seems to be sort of honing in on that you think may have been responsible for the delay? Or where they wanted to -- there were sort of a couple of one or two major questions that they wanted answers to or wanted a little bit more time to analyze the data around? Or, should we think about the delay as really, look, this is just, it's a complex data set, it's a new disease to them, they just need more time? Like, I guess, how confident are you that there aren't a few different, one or two major sticking points with the agency at this point?
>
> A - Shoshana Shendelman: *{FS24}* **We actually don't think that there are any major sticking points with the agency**. We just believe there is a six-month review for a first-in-disease state asset, so this is the first drug ever developed and under review by the FDA for Galactosemia. *{FS25}* **So, we don't think that there are any sticking points**. *{FS26}* **We did meet very collaboratively with the FDA prior to submitting our NDA. And we asked them very openly if the data we had generated was acceptable for a potential submission and approval. We wouldn't have submitted otherwise if their answer was no.**
>
> *{FS27}* **And I think that, the NDA acceptance and the positive interactions that we've had have also provided a lot of additional comfort there. So, we feel very good about their review. We don't think that there are any big issues**. We think it's all a risk-benefit analysis, with diseases like Galactosemia. *{FS28}* **And with Govorestat having a very positive safety profile, we think the risks are very low. And then we look to the benefit. And I think the benefit that we have**

demonstrated in our clinical studies is very clear and substantial, and clinically meaningful to parents and to patients. And so, we're very confident in the process and we're very hopeful that this will be the first drug approved for Galactosemia later this year.

Q - Brian Abrahams: Good. How has your communication been with the agency since the announcement of the delay?

A - Shoshana Shendelman: *{FS29}* **It's been very positive and sort of normal course.**

Q - Brian Abrahams: Good. It sounds like the FDA is likely to convene in AdComm to discuss the drug, as one might expect for a first -- in class-first indication. I guess, what would your expectations be with regards to potential timing of when the FDA might assemble this committee? I know there isn't a Standing Committee necessarily with this division. What does that mean? And what would you expect the key discussion points would be once this is put before an AdComm?

A - Shoshana Shendelman: We are anticipating an AdComm, although we don't have a date for it yet. So, that's something we're watching for as well from the FDA. And we believe that, and I think this has been publicly stated by Bob Califf, that they are moving towards having Advisory Committee Meetings for diseases, where it's the first-in-class, first in disease state, which is clearly the case for Galactosemia. And that they would like to see those discussions really focused on risk-benefit. *{FS30}* **So, our anticipation is that if there is an AdComm, it will really be a risk-benefit analysis, which is very similar to the conversations that we've been having with FDA.**

171. When asked whether any non-clinical or manufacturing work remained, Dr. Shendelman responded: "We've met all of those points. So, I think, we're in great shape. There's nothing really outstanding that we have."

Q - Brian Abrahams: Any additional non-clinical or other work that needs to be done ahead of the PDUFA to satisfy all the requirements for the FDA? And can you talk about—if so, can you talk about any progress on those fronts?

A - Shoshana Shendelman: I think just like any program that's under review, there are certain points that you need to hit from a manufacturing perspective, from an informational perspective along the review timeline. We've met all of those points. So, *{FS31}* **I think, we're in great shape. There's nothing really outstanding that we have** --

172. FS21 through FS31 were materially false and misleading in violation of Section 10(b) and Rule 10b-5 because they contained untrue statements of material fact or omitted to state

material facts necessary in order to make the statements made not misleading. Specifically, at the time these statements were made, Dr. Shendelman and Applied were aware of, or were severely reckless in not knowing, that (a) FDA regulations required the NDA to include "a description and analysis of any other data or information relevant to an evaluation of the safety and effectiveness of [govorestat] obtained or otherwise received by [Applied] from any source…including information derived from clinical investigations," (b) that the Dosing Errors and Dosing Errors Clinical Data was such "other data or information," (c) that in the NDA, Applied failed to provide the FDA with a description or analysis of the Dosing Errors or the Dosing Errors Clinical Data, and (d) that instead, as the FDA subsequently stated, "reported dose levels for subjects as stated in the protocol…rather than the actual dose levels administered."

173. Further, Defendants knew, or recklessly disregarded, that they would be, and in fact had already been, subject to an FDA investigation in connection with the NDA, and as such there was a significant risk that the Dosing Errors and Dosing Errors Clinical Data would be discovered by the FDA. As such, these undisclosed facts were negative material factors and a significant risk that the FDA would not approve the NDA because they raised significant concerns about the validity, reliability, and integrity of the clinical data and Applied's oversight and conduct of its clinical investigations.

174. FS21 through FS31 were also materially false and misleading in violation of Section 10(b) and Rule 10b-5 because, at the time these statements were made, Dr. Shendelman and Applied were aware of, or were severely reckless in not knowing, that (a) Applied had informed the FDA that electronic source data for 11 subjects in the Pediatric Study had been deleted and not been recovered, (b) as a result, this data could not be verified by the FDA as part of its investigation, which raised concerns about the validity and integrity of the data collected

during the Pediatric Study, (c) that Applied, the NDA, and Pediatric Study were in violation of 21 C.F.R. § 312.58 and the terms of the protocol for the Pediatric Study; (d) that Applied could not rectify the "objectionable condition" identified by the FDA of the deletion of the electronic clinical data for 11 test subjects; (e) that these facts, in addition to the omission of the Dosing Errors and Dosing Errors Clinical Data from the NDA, were a serious and material risk that the FDA would reject the NDA; and (f) that there existed a serious and material negative development for the Company's prospects for NDA approval and ability to commercialize govorestat.

175. By failing to disclose these material facts, Dr. Shendelman and Applied misled investors and the public, who as a result, reasonably believed that (a) the NDA complied with FDA regulations, (b) the NDA contained all required information and clinical results from the Pediatric Study, (c) the NDA accurately reported the clinical data Applied obtained for the study, (d) the FDA had not identified, and Defendants were not aware of, any issues with the NDA or the clinical data underlying the NDA, and (e) there were no known material risks to approval of the NDA, when in fact this was not true.

176. For these reasons related to the Dosing Errors and the Study Data Deletion, Dr. Shendelman and Applied did not have a reasonable basis to speak concerning interactions with the FDA, likelihood of approval of the NDA, and commercialization of govorestat, and once they chose to speak concerning these topics, had a duty to disclose all material facts concerning those subjects to ensure that a reasonable investor would not be misled.

177. FS21 through FS31 were also materially false and misleading in violation of Section 10(b) and Rule 10b-5 because they led investors to believe that all clinical data for the Pediatric Study had been discussed with the FDA, and that there were no problems with that data. However, this was not true, because Applied had omitted information about the Dosing Errors and

the Dosing Errors Clinical Data from the NDA, and the FDA was not able to verify all clinical data for the Pediatric Study due to the Study Data Deletion.

c) Defendants Made Materially False and Misleading Statements at the June 6, 2024 Annual Meeting and in a July 1, 2024 Press Release About the Russell 3000 Index Concerning the NDA and the Commercialization of Govorestat

178. On June 6, 2024, at approximately 10:00 a.m. ET, the Company held its annual meeting of stockholders in virtual meeting format. A transcript of the annual meeting of stockholders was prepared and distributed by Bloomberg.

179. Officers and directors of Applied who attended the annual meeting included Dr. Shendelman and Dr. Perfetti.

180. At the annual meeting, Dr. Shendelman gave a "recap of the past year," including a discussion of the NDA and the Company's interactions with the FDA concerning the NDA:

> *{FS32}* **With potential approvals on the horizon, we are continuing to prepare for commercial launch of govorestat and have built a strong commercial and operational team**. We believe govorestat has the potential to greatly impact patients with Galactosemia, and *{FS33}* **we look forward to potentially making this drug available to patients later this year in the U.S., and in early 2025 in the EU**.

181. Also on June 6, 2024, Dr. Shendelman sold 61,795 shares of Applied common stock, 0.76% of her total holdings at the time, at the artificially inflated price of $4.32, for proceeds of $366,954.40.

182. On July 1, 2024, during pre-market hours, the Company issued a press release titled "Applied Therapeutics Added to Russell 3000® Index" (the "7/1/2024 Press Release"). Dr. Shendelman was quoted in the 7/1/2024 Press Release:

> The addition of Applied to the Russell 3000® index underscores the progress we have made as a publicly traded company with a core mission of addressing diseases with no treatment options…*{FS34}* **We are at a pivotal time for the company with multiple key value-generating milestones upcoming. We look forward to providing regulatory updates this year for govorestat for the potential**

treatment of Classic Galactosemia and SORD Deficiency, both progressive rare diseases that represent significant opportunities to address patient needs.

183. FS32 through FS34 were materially false and misleading in violation of Section 10(b) and Rule 10b-5 because they contained untrue statements of material fact or omitted to state material facts necessary in order to make the statements made not misleading. Specifically, at the time these statements were made, Dr. Shendelman and Applied were aware of, or were severely reckless in not knowing, that (a) FDA regulations required the NDA to include "a description and analysis of any other data or information relevant to an evaluation of the safety and effectiveness of [govorestat] obtained or otherwise received by [Applied] from any source…including information derived from clinical investigations," (b) that the Dosing Errors and Dosing Errors Clinical Data was such "other data or information," (c) that in the NDA, Applied failed to provide the FDA with a description or analysis of the Dosing Errors or the Dosing Errors Clinical Data, and (d) that instead, as the FDA subsequently stated, "reported dose levels for subjects as stated in the protocol…rather than the actual dose levels administered."

184. Further, Defendants knew, or recklessly disregarded, that they would be, and in fact had already been, subject to an FDA investigation in connection with the NDA, and as such there was a significant risk that the Dosing Errors and Dosing Errors Clinical Data would be discovered by the FDA. As such, these undisclosed facts were negative material factors and a significant risk that the FDA would not approve the NDA because they raised significant concerns about the validity, reliability, and integrity of the clinical data and Applied's oversight and conduct of its clinical investigations.

185. FS32 through FS34 were also materially false and misleading in violation of Section 10(b) and Rule 10b-5 because, at the time these statements were made, Dr. Shendelman and Applied were aware of, or were severely reckless in not knowing, that (a) Applied had

informed the FDA that electronic source data for 11 subjects in the Pediatric Study had been deleted and not been recovered, (b) as a result, this data could not be verified by the FDA as part of its investigation, which raised concerns about the validity and integrity of the data collected during the Pediatric Study, (c) that Applied, the NDA, and Pediatric Study were in violation of 21 C.F.R. § 312.58 and the terms of the protocol for the Pediatric Study; (d) that Applied could not rectify the "objectionable condition" identified by the FDA of the deletion of the electronic clinical data for 11 test subjects; (e) that these facts, in addition to the omission of the Dosing Errors and Dosing Errors Clinical Data from the NDA, were a serious and material risk that the FDA would reject the NDA; and (f) that there existed a serious and material negative development for the Company's prospects for NDA approval and ability to commercialize govorestat.

186. By failing to disclose these material facts, Dr. Shendelman and Applied misled investors and the public, who as a result, reasonably believed that (a) the NDA complied with FDA regulations, (b) the NDA contained all required information and clinical results from the Pediatric Study, (c) the NDA accurately reported the clinical data Applied obtained for the study, (d) the FDA had not identified, and Defendants were not aware of, any issues with the NDA or the clinical data underlying the NDA, and (e) there were no known material risks to approval of the NDA, when in fact this was not true.

187. For these reasons related to the Dosing Errors and the Study Data Deletion, Dr. Shendelman and Applied did not have a reasonable basis to speak concerning the likelihood of approval of the NDA or commercialization of govorestat, and once they chose to speak concerning these issues, had a duty to disclose all material facts concerning those subjects to ensure that a reasonable investor would not be misled.

188. FS34 was also materially false and misleading in violation of Section 10(b) and Rule 10b-5 because when stating that "we look forward to providing regulatory updates," Dr. Shendelman and Applied led the market to believe that there were no regulatory updates, when the opposite was true due to the Form 483, the Study Data Deletion, and Applied telling the FDA that clinical data for 11 subjects could not be recovered.

189. Also, Dr. Shendelman's and Applied's statement that it was a "a pivotal time for the company with multiple key value-generating milestones upcoming," was a half-truth. Once Dr. Shendelman discussed upcoming "value generating milestones," she had a duty to disclose the whole truth, including that the Study Data Deletion had occurred, the FDA had learned of the Study Data Deletion, Applied had received a Form 483, Applied had responded to that Form 483, and there was a serious material negative factor standing in the way of approval of the NDA and the commercialization of govorestat (the value generating milestone).

190. On August 2, 2024, analyst William Blair & Co. initiated coverage of Applied with a recommendation of outperform and a fair value of Applied shares at $14 per share, stating the Company was an "under-the-radar company developing a nice mix of therapeutics targeting rare diseases and some larger indications with potential for several major value inflections over the next 12 months." William Blair also anticipated that Applied would launch govorestat (*i.e.*, the NDA would be approved) in the galactosemia market in 2025.

d) Defendants' August 7, 2024 Press Release, Form 8-K, and Form 10-K Concerning Applied's Second Quarter 2022 Financial Results Contained Materially False and Misleading Statements Regarding the NDA and Commercialization of Govorestat, and Provide a Positive Data Recalculation Update Without Also Disclosing Known Negative Factors for the NDA's Approval

191. On August 7, 2024, during pre-market hours, the Company issued a press release titled "Applied Therapeutics Reports Second Quarter 2024 Financial Results" (the "8/7/2024 Press

Release"). Also on August 7, 2024, during pre-market hours, the Company filed a Form 8-K with the SEC that attached the 8/7/2024 Press Release as an exhibit (the "8/7/2024 Form 8-K"). The 8/7/2024 Form 8-K was signed by Dr. Shendelman.

192. In addition, on August 7, 2024, during pre-market hours, the Company filed its Form 10-Q for the second fiscal quarter of 2024 ending June 30, 2024 with the SEC (the "2Q 2024 Form 10-Q"). The 2Q 2024 Form 10-Q was signed by Dr. Shendelman and Mr. Funtleyder.

193. The 8/7/2024 Press Release and 2Q 2024 Form 10-Q (at 29) both restated FS1, which was false and misleading for the reasons stated in paragraphs 80-82:

> *{FS1}* **The NDA and MAA submission packages include clinical outcomes data from the Phase 3 registrational ACTION-Galactosemia Kids study in children age[d] 2-17 with Galactosemia, the Phase 1/2 ACTION-Galactosemia study in adult patients with Galactosemia, and preclinical data.**

194. The 8/7/2024 Press Release also restated FS17, which was false and misleading for the reasons stated in paragraphs 158-163:

> *{FS17}* **Additionally, the Company expects that the sale of the priority review voucher (PRV), which would be granted upon a potential NDA approval of govorestat for the treatment of Galactosemia, could substantially extend the Company's cash runway.**

195. The 8/7/2024 Press Release also provided a positive update on the NDA and the clinical data underlying the NDA:

> *{FS35}* **In the process of preparing for the United States Food and Drug Administration (FDA) inspection, it was discovered that the vendor hired to compile NIH Toolbox data for the Company used an adult formula for calculation of about one third of composite cognition and motor skills scores. Adjusting the formula to the pediatric formula resulted in significantly improved data for cognition as compared to the prior data, demonstrating improvement in the govorestat (AT-007) treated group of approximately 8 points on a standard scale, which was statistically significant compared to placebo (p=0.032). This also resulted in a statistically significant effect on the primary endpoint sensitivity analysis which included cognition (p=0.034). The motor skills data did not change substantially. These updates were disclosed and discussed with the FDA and European Medicines Agency (EMA) and will**

be used in the ongoing evaluation of the New Drug Application (NDA) and Marketing Authorization Application (MAA).

196. The 2Q 2024 Form 10-Q contained a substantially similar positive update statement:

> *{FS36}* In Q2, **in the process of preparing for FDA inspection, it was discovered that the vendor we engaged to compile NIH Toolbox data for the Company used an adult formula for calculation of about one third of composite cognition and motor skills scores. Adjusting the formula to the pediatric formula resulted in significantly improved data for cognition as compared to the prior data, demonstrating improvement in the govorestat treated group of approximately 8 points on a standard scale, which was statistically significant compared to placebo (p=0.032). This also resulted in a statistically significant effect on the primary endpoint sensitivity analysis which included cognition (p=0.034). The motor skills data did not change substantially. These updates were disclosed and discussed with the FDA and EMA and will be used in the ongoing evaluation of the NDA and MAA.**

197. FS35 and FS36 were materially false and misleading in violation of Section 10(b) and Rule 10b-5 at the time they were made because they contained untrue statements of material fact or omitted to state material facts necessary in order to make the statements made, in the light of the circumstances under which they were made, not misleading. Once Dr. Shendelman and Applied decided to disclose a data reanalysis of the clinical data underlying the NDA, linked that reanalysis to preparation for a FDA inspection, and frame it as a ***positive*** development, Dr. Shendelman and Applied had an obligation to disclose the whole truth, including the ***negative*** factor related to a FDA inspection that they were aware of – the Study Data Deletion, the Form 483, and that source data for 11 trial participants had been deleted, could not be recovered, and could not be verified by the FDA – as well as the fact that they knew that the NDA omitted other information – the Dosing Errors and Dosing Errors Clinical Data – that were required to be included in the NDA and that the FDA would also find material to its evaluation of the NDA. By omitting this information, Dr. Shendelman and Applied deceived the investing public into thinking that there were only positive developments, when they knew about negative developments.

198. Dr. Shendelman was quoted in the 8/7/2024 Press Release as stating:

> *{FS37}* **Momentum continues with our steady regulatory progress in Classic Galactosemia and SORD Deficiency**…At Applied, we are dedicated to creating transformative treatments for rare diseases, and *{FS38}* **we continue to work closely with regulatory agencies and patient advocacy groups to ensure that treatments become available for patients with these debilitating diseases.**

199. FS35 through FS38 were materially false and misleading in violation of Section 10(b) and Rule 10b-5 because they contained untrue statements of material fact or omitted to state material facts necessary in order to make the statements made not misleading. Specifically, at the time these statements were made, Dr. Shendelman and Applied were aware of, or were severely reckless in not knowing, that (a) FDA regulations required the NDA to include "a description and analysis of any other data or information relevant to an evaluation of the safety and effectiveness of [govorestat] obtained or otherwise received by [Applied] from any source…including information derived from clinical investigations," (b) that the Dosing Errors and Dosing Errors Clinical Data was such "other data or information," (c) that in the NDA, Applied failed to provide the FDA with a description or analysis of the Dosing Errors or the Dosing Errors Clinical Data, and (d) that instead, as the FDA subsequently stated, "reported dose levels for subjects as stated in the protocol…rather than the actual dose levels administered."

200. Further, Defendants knew, or recklessly disregarded, that they would be, and in fact had already been, subject to an FDA investigation in connection with the NDA, and as such there was a significant risk that the Dosing Errors and Dosing Errors Clinical Data would be discovered by the FDA. As such, these undisclosed facts were negative material factors and a significant risk that the FDA would not approve the NDA because they raised significant concerns about the validity, reliability, and integrity of the clinical data and Applied's oversight and conduct of its clinical investigations.

201. FS35 through FS38 were also materially false and misleading in violation of Section 10(b) and Rule 10b-5 because, at the time these statements were made, Dr. Shendelman and Applied were aware of, or were severely reckless in not knowing, that (a) Applied had informed the FDA that electronic source data for 11 subjects in the Pediatric Study had been deleted and not been recovered, (b) as a result, this data could not be verified by the FDA as part of its investigation, which raised concerns about the validity and integrity of the data collected during the Pediatric Study, (c) that Applied, the NDA, and Pediatric Study were in violation of 21 C.F.R. § 312.58 and the terms of the protocol for the Pediatric Study; (d) that Applied could not rectify the "objectionable condition" identified by the FDA of the deletion of the electronic clinical data for 11 test subjects; (e) that these facts, in addition to the omission of the Dosing Errors and Dosing Errors Clinical Data from the NDA, were a serious and material risk that the FDA would reject the NDA; and (f) that there existed a serious and material negative development for the Company's prospects for NDA approval and ability to commercialize govorestat.

202. By failing to disclose these material facts, Dr. Shendelman and Applied misled investors and the public, who as a result, reasonably believed that (a) the NDA complied with FDA regulations, (b) the NDA contained all required information and clinical results from the Pediatric Study, (c) the NDA accurately reported the clinical data Applied obtained for the study, (d) the FDA had not identified, and Defendants were not aware of, any issues with the NDA or the clinical data underlying the NDA, and (e) there were no known material risks to approval of the NDA, when in fact this was not true.

203. For these reasons related to the Dosing Errors and the Study Data Deletion, Dr. Shendelman and Applied did not have a reasonable basis to speak concerning regulatory progress and the likelihood of approval of the NDA and commercialization of govorestat, and once they

chose to speak concerning these topics and regulatory updates, had a duty to disclose all material facts concerning those subjects to ensure that a reasonable investor would not be misled.

204. The 2Q 2024 Form 10-Q (at 50) also restated the risk factor FS19 from the 1Q 2024 Form 10-Q, which was false and misleading for the reasons stated in paragraph 165:

> Prior to obtaining approval to commercialize any product candidate in the United States or abroad, *{FS19}* **we must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA or comparable foreign regulatory authorities, that such product candidate is safe and effective for its intended uses.**

205. Attached to the 2Q 2024 Form 10-Q as Exhibit 31.1 was a signed certification, dated August 7, 2024, by Dr. Shendelman pursuant to the Sarbanes Oxley Act stating:

> I have reviewed this Form 10-Q of Applied Therapeutics, Inc.;
>
> *{FS39}* **Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report**.

206. FS39 was materially false and misleading in violation of Section 10(b) and Rule 10b-5 because it was an untrue statement of fact. Dr. Shendelman knew that FS1, FS19, FS36 were included in the 2Q 2024 Form 10-Q and were materially false and misleading.

207. Defendants' statements reassured analysts and investors that the data reanalysis disclosed on August 7, 2024 was a positive development and an isolated incident. For example, RBC Capital Markets issued a report that stated:

> we had a chance to catch up with the mgmt. team. With a favorable data reanalysis . . . **we see favorable tailwinds for govorestat in galactosemia into the Oct 9 panel and Nov 28 PDUFA** . . . . The company announced corrections to the formula used for their cognition and motor skill scores (initially had used adult, vs pediatric formula) from the ph.III galactosemia trial, resulting in improvement on a sensitivity analysis of the primary endpoint including cognition (cognition turned stat. sig.) **We believe this may incrementally strengthen APLT's data package in anticipation of their AdComm** [Advisory Committee] – especially given GeMDAC's recent emphasis of the importance of cognition for a recently reviewed

> drug. *{FS40}* **While this delayed error identification may lead to questions about whether there may be additional mistakes in the rest of the data package (recall data integrity and presentation had been a concern for some), the company emphasized that this is isolated to a single toolbox of tests done by a third party and that their careful audit of the rest of the package did not reveal any other discrepancies.**

208. FS40 was materially false and misleading in violation of Section 10(b) and Rule 10b-5 for the same reasons as FS35 through FS38. Applied statement, made through its management (Dr. Shendelman or Dr. Perfetti), and disseminated by RBC Capital Markets, that it had done a "careful audit of the rest of the [NDA] package" that "did not reveal any other discrepancies" falsely re-assured the market that there were no "additional mistakes" such as data integrity. However, the opposite was true. Defendants were aware that the NDA failed to include information about the Dosing Errors and Dosing Errors Clinical Data, and that electronic source data for 11 test subjects had been deleted and could not be recovered, and as such the FDA could not verify this test data.

7. Dr. Shendelman Sold 777,014 Shares of Applied Common Stock Between August 12 and 14, 2024, for Net Proceeds of Over $4.7 Million, While Knowing of the Dosing Errors, the Study Data Deletion, and the Form 483

209. On August 9, 2024, after Dr. Shendelman received the Form 483 concerning the Study Data Deletion, after Applied responded to the From 483, and while she was aware of the Dosing Errors and that the NDA failed to include information about the Dosing Errors in violation of FDA regulations, Dr. Shendelman executed a Form 144, Notice of Proposed Sale of Securities, that was filed with the SEC. The Form 144 stated that she intended to sell 1 million shares of Applied common stock with an aggregate market value of $6.21 million on August 12, 2024.

210. On August 12, 2024, Dr. Shendelman sold 300,000 shares of Applied common stock at the artificially inflated average sales price of $5.98 per share and for total proceeds of $1,794,000.

211. On August 13, 2024, Dr. Shendelman sold 357,423 shares of Applied common stock at the artificially inflated average price of $6.18 per share and for total proceeds of $2,208,874.14.

212. On August 14, 2024, Dr. Shendelman sold 119,591 shares of Applied common stock at the artificially inflated average price of $5.93 per share and for total proceeds of $709,174.63.

213. In total, over the three day period August 12, 2024 to August 14, 2024, Dr. Shendelman sold 777,014 shares of Applied shares for net proceeds of $4,712,048.63.

214. According to a Form 13D-A filed by Dr. Shendelman with the SEC on August 14, 2024, after these sales were complete, Dr. Shendelman owned or controlled 7,803,355 shares of Applied common stock, including "86,988 shares of Common Stock underlying restricted stock units that will vest within 60 days of August 14, 2024 and (d) 3,079,734 shares of Common Stock underlying outstanding options that are immediately exercisable or will be immediately exercisable within 60 days of August 14, 2024."

215. Dr. Shendelman's sales of common stock on August 12-14, 2024 were made when she was in possession of material nonpublic information about the Dosing Errors, the Study Data Deletion, the Form 483, and the FDA's concerns with the Study Data Deletion.

216. Dr. Shendelman's sales of common stock on August 12-14, 2024 were equal to over 9% of her Applied holdings before those sales took place, calculated as 777,014 shares sold divided by the sum of 777,014 shares sold plus 7,803,355 shares owned or controlled after the sales.

8. In August and September 2024, Applied and the FDA Exchanged Letters Concerning the Study Data Deletion, Further Evidencing Defendants' Knowledge of the Seriousness of the Study Data Deletion and the FDA's Concerns

217. On August 20, 2024, the FDA sent the Company a follow up "Information Request concerning the Study Data Deletion.

218. On August 27, 2024, Applied responded in writing to the Information Request, and stated that "an export of the [**redacted**] data from the backup Q-global® system is maintained with a third-party statistical consulting vendor; however, the data is no longer available in Q-global®." Warning Letter at 3.

219. On September 5, 2024, the FDA sent Applied correspondence providing the Late Cycle Meeting Background Package and that concerned the Study Data Deletion issues. Warning Letter at 3.

220. On September 11, 2024, Applied provided a written response to the FDA's September 5, 2024 correspondence. The Company stated that the third-party vendor deleted the data study from the Q-global system without consulting Applied and that it was able to recover this data from the Q-global system's backup, except for 11 tests. Applied noted that, before the electronic data's deletion, item-level responses were captured in PDF and in paper copies of the score reports.

> Applied Therapeutics stated that the third-party vendor deleted the data [**redacted**] from the Q-global® system without consulting Applied Therapeutics, the sponsor. Applied Therapeutics also stated that it was able to recover this data from the Q-global® system's backup, except for the 11 [**redacted**] tests. Applied Therapeutics noted that, before the electronic data's deletion, item-level responses were captured in PDF and in paper copies of the score reports.

221. As disclosed later in the Warning Letter, the Company's response was inadequate because it did not include sufficient details about its corrective action plan. For example, it did not provide sufficient details regarding the procedures being implemented to prevent similar violations

in the future. Additionally, the FDA remained concerned that electronic data collected for critical eCOAs was deleted and could not be verified, which raised concerns about the validity and integrity of the data collected during the clinical investigation of govorestat. Without access to the pertinent electronic data in Q-global, including associated audit trails, FDA could not verify the accuracy, consistency, and completeness of study data collected for critical eCOAs used to measure primary and secondary efficacy endpoints, and could not evaluate the extent and impact of any reported data errors and discrepancies. Accordingly, the FDA could not confirm whether the clinical investigation of govorestat was conducted in compliance with federal law or the study's protocol.

222. The FDA communications and the Company's responses concerning the Form 483 and the Study Data Deletion were not disclosed to investors during the Class Period.

9. Defendants Made Additional False and Misleading Statements in the Fall of 2024 with Knowledge of the Dosing Errors and the Study Data Deletion

a) Dr. Perfetti Made Materially False and Misleading Statements Concerning the Results of the Pediatric Study in a September 4, 2024 Presentation

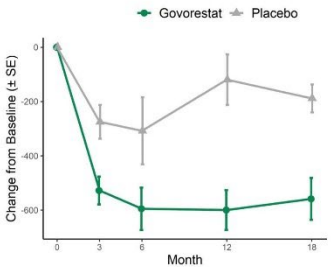
223. On September 4, 2024, Dr. Perfetti and Dr. Bailey presented with Barbara Burton, MD, Professor of Pediatrics, Genetics, Genomics and Metabolism at the Northwestern University Feinberg School of Medicine, at the 2024 Annual Symposium of the Society for the Study of Inborn Errors of Metabolism ("SSIEM Symposium") on "Development of Govorestat (AT-007), the First Potential Treatment for Patients with Classic Galactosemia" (the "9/4/2024 Presentation"). A copy of the 9/4/2024 Presentation was published on Applied's website. Both Dr. Perfetti and Dr. Bailey had their biographies on the first few slides of the 9/4/2024 Presentation and were the authors or presenters of the slides discussed below.

224. *{FS41}* Slides 40 and 42 through 55 of the 9/4/2024 Presentation contained statements regarding the results of the Pediatric Study, including the dosages given and the clinical results achieved:

Govorestat Treatment Reduced Plasma Galactitol Levels by 40% (p<0.001 vs. placebo)

Galactitol reduction began on the first day of treatment, and was sustained over 18 months

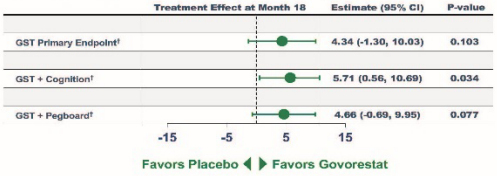
Weight Group	Govorestat Dose (QD)	% Galactitol Reduction From Baseline
>40kg	15mg/kg	38.29%
20-40kg	20mg/kg	41.43%
<20kg	30mg/kg	39.83%
All groups	**15-30mg/kg**	**40.19% (p<0.001)**



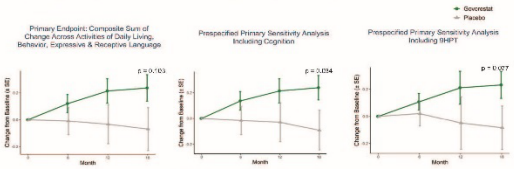
No compensatory increase in galactose or Gal-1p

APPLIED THERAPEUTICS Perfetti et al. 2022 Annual Meeting SIMD Presentation: Baseline Disease Characteristics of 47 Pediatric Classic Galactosemia Patients in the ACTION-Galactosemia KIDS AT-007 Interventional Study Demonstrate the Multi-System Burden of Disease.

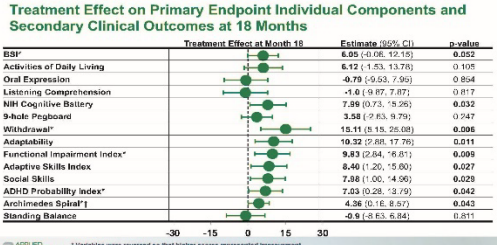
Primary Endpoint and Primary Endpoint Sensitivity Results Favor Govorestat; Sensitivity Analysis Including Cognition Statistically Significant



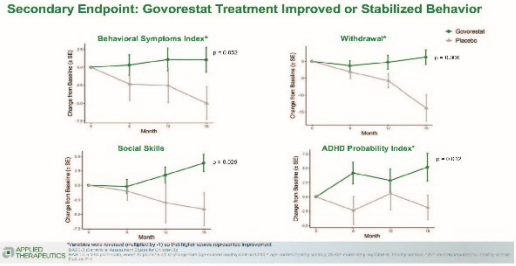
Govorestat Treatment Benefit Increases Over Time Primary Endpoint and Sensitivity Analyses at 6, 12 and 18 Months

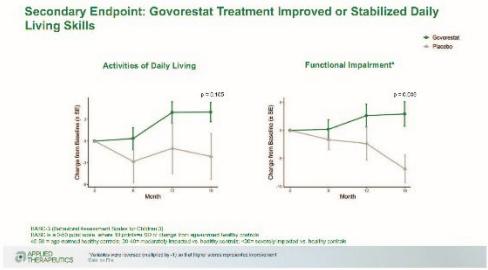


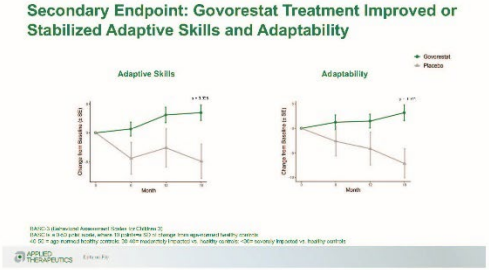
Treatment Effect on Primary Endpoint Individual Components and Secondary Clinical Outcomes at 18 Months

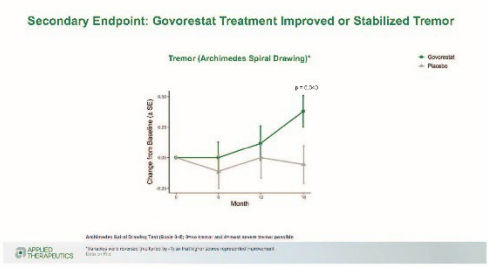


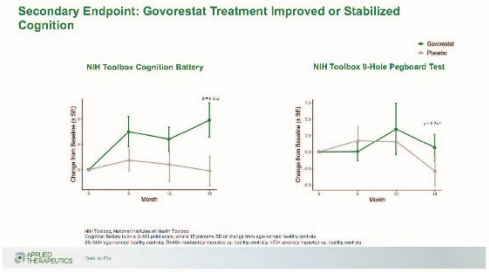
Secondary Endpoint: Govorestat Treatment Improved or Stabilized Behavior

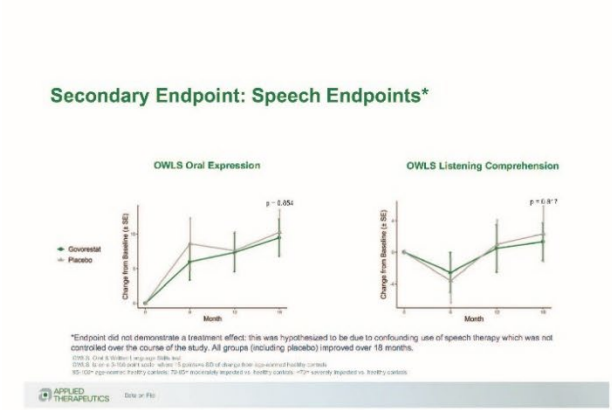


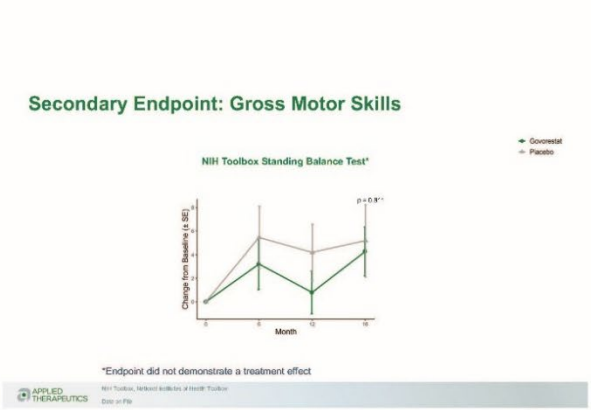

Secondary Endpoint: Govorestat Treatment Improved or Stabilized Daily Living Skills
Govorestat
Placebo
Activities of Daily Living
Functional Impairment*
Change from Baseline (± SE)
Month
APPLIED THERAPEUTICS

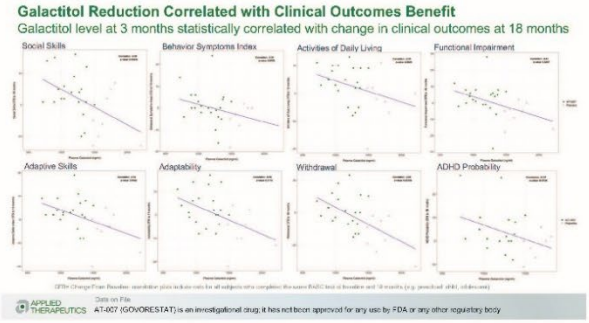

Secondary Endpoint: Govorestat Treatment Improved or Stabilized Adaptive Skills and Adaptability
Govorestat
Placebo
Adaptive Skills
Adaptability
Change from Baseline (± SE)
Month
APPLIED THERAPEUTICS

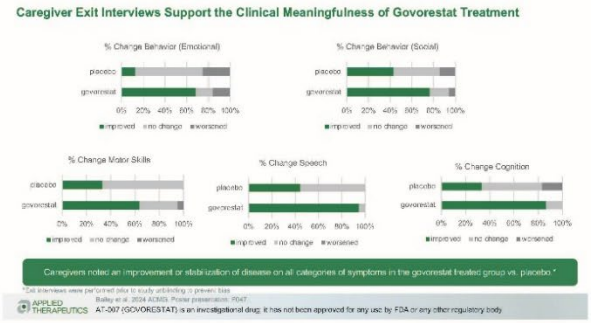

Secondary Endpoint: Govorestat Treatment Improved or Stabilized Tremor
Tremor (Archimedes Spiral Drawing)*
Govorestat
Placebo
Change from Baseline (± SE)
Month
APPLIED THERAPEUTICS


Secondary Endpoint: Govorestat Treatment Improved or Stabilized Cognition
Govorestat
Placebo
NIH Toolbox Cognition Battery
NIH Toolbox 9-Hole Pegboard Test
Change from Baseline (± SE)
Month
APPLIED THERAPEUTICS









Safety Summary

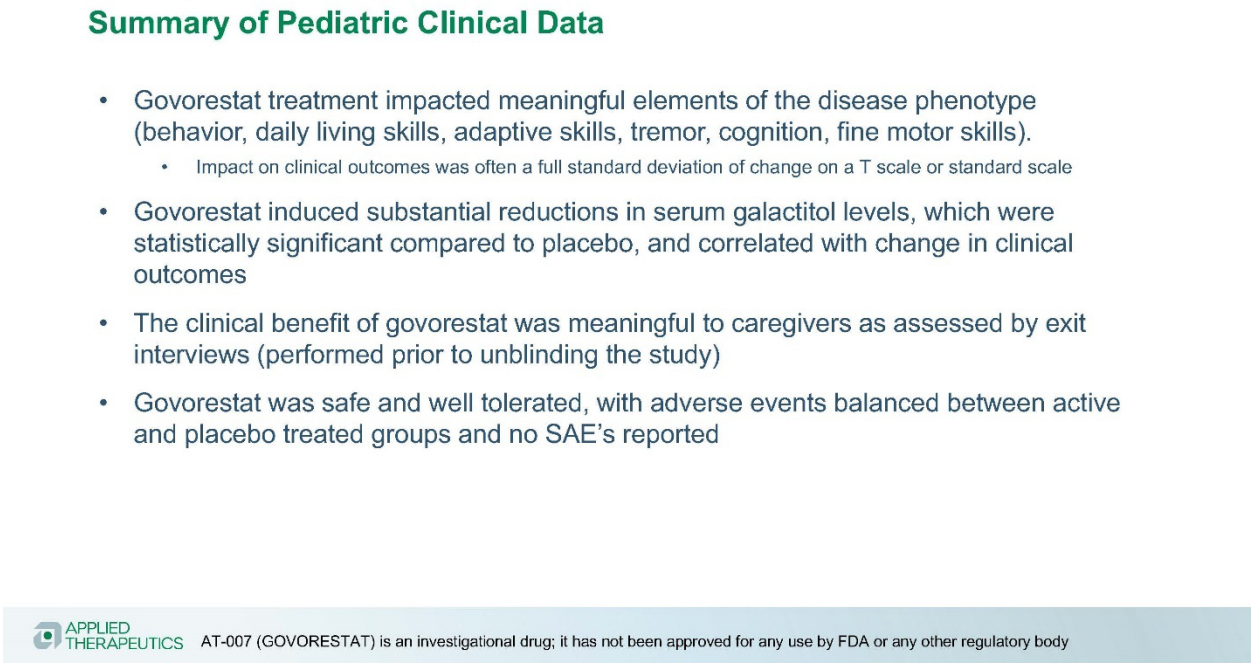
- Govorestat was safe and well-tolerated with no serious adverse events
- All adverse events were mild to moderate
- Adverse events & lab values were generally balanced between govorestat and placebo groups
  - Slightly higher incidence elevated ALT/AST in govorestat-treated patients; all were reversible – no bilirubin increase (no Hy's Law cases)

AE, n (%)	Placebo (n=16)	Govorestat (n=31)
Gastrointestinal disorders	11 (68.8)	23 (74.2)
Vomiting	5 (31.3)	15 (48.4)
Diarrhea	2 (12.5)	8 (25.8)
Hepatic enzyme increased (ALT/AST)	2 (12.5)	8 (25.8)
Urine albumin/creatinine ratio increased*	7 (43.8)	5 (16.1)
Urine protein/creatinine ratio increased*	3 (18.8)	2 (6.5)
Infections and infestations	10 (62.5)	18 (58.1)
Viral upper respiratory tract infection	3 (18.8)	14 (45.2)

*Govorestat interferes with the colorimetric assay to measure serum creatinine. Any elevation in serum creatinine during the study was due to this and confirmed to be normal on repeat using the enzymatic assay to measure serum creatinine. As such, there were no elevations in serum creatinine nor cases of Acute Kidney Injury in the study.

APPLIED THERAPEUTICS Data on File

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate transaminase; TEAE, treatment emergent adverse event; Refers to patients having reported at least 1 term in AE category.



225. FS41 was materially false and misleading in violation of Section 10(b) and Rule 10b-5 at the time it was made because the slides contained untrue statements of material fact or omitted to state material facts necessary in order to make the statements made, in the light of the circumstances under which they were made, not misleading. At the time the slides were published, Dr. Perfetti and Applied knew that there were additional clinical results for the Pediatric Study that were not disclosed in FS41 or the NDA, namely the Dosing Errors Clinical Data. Reasonable investors would conclude that the results included in the 9/4/2024 Presentation were the same results that were used to support the NDA. By failing to disclose the Dosing Errors or the Dosing Errors Clinical Data, Defendants led investors to believe that the results described above were the complete results of the Pediatric Study, and there were no other results from the study that were required to be included in the NDA. Defendants further led investors to believe that the clinical data in the 9/4/2024 Presentation was verifiable, when in fact it was not due to the Study Data Deletion.

b) Dr. Shendelman Made Materially False and Misleading Statements at the September 10, 2024 Baird Global Healthcare Conference Concerning Approval of the NDA

226. On September 10, 2024, at approximately 3:45 p.m. ET, Dr. Shendelman participated on behalf of the Company in a fireside chat at the Baird 2024 Global Healthcare Conference. Dr. Shendelman used a slide presentation at the Baird 2024 Global Healthcare Conference, but that presentation has not been publicly disclosed.

227. At the Baird 2024 Global Healthcare Conference, Dr. Shendelman was asked by Brian Skorney, one of Baird's senior biotech analysts, "could you give us a little bit of an overview of what Applied is doing these days?" Shendelman responded:

> Yes, absolutely. I have a tutorial on the slide too. So this is our pipeline. Applied Therapeutics is developing drugs for rare diseases, specifically rare diseases that have no treatments available. So our drug, govorestat, which Brian mentioned, is under FDA and EMA review right now for a rare disease called galactosemia, *{FS42}* **is advancing towards hopeful potential approval**.
>
> Our PDUFA date is November 28 and we have a second rare disease indication right behind it, called SORD deficiency, which is a neuromuscular rare disease. We have plans to submit our NDA in SORD deficiency under accelerated approval in the first quarter of next year. Both indications, again have no treatments available, and *{FS43}* **so this is an opportunity to be the first drug approved for both indications**.

228. Later in the discussion, Skorney asked Dr. Shendelman about the status of the NDA and the approval timeline with the FDA for the NDA:

> Q - Brian Skorney: Right? So now you have an NDA, it's been accepted. You have priority review. There's a tentative Advisory Committee scheduled for October 9, I guess. How should we be thinking about that date? At what point do you think that gets in the Federal Regist[er] and is set in stone, and what are you hearing from the FDA in terms of the timeline for confirming that? And what sort of your plan? What do you think are going to be the major questions the FDA has for the company?
>
> A - Shoshana Shendelman: … So we've been preparing basically the whole summer for the Advisory Committee Meeting. *{FS44}* **I think we're in great shape, just noting that it's tentative and remains to be confirmed**. We have our

late-cycle meeting with the FDA very soon. So our understanding is that we'll receive an update there.

229. Later on, when discussing the Advisory Committee Meeting, Dr. Shendelman stated that:

> And that when there's an urgency to treat, as we believe is the case with galactosemia, it's a progressive disease, it affects children, there are no drugs approved, and we have a favorable safety and efficacy profile, our hope is that that same flexibility that they've shown with that last Advisory Committee meeting really applies to our program as well, and *{FS45}* **we see an approval in galactosemia in the near term.**

230. Skorney also asked Dr. Shendelman about the commercialization of govorestat:

> Q - Brian Skorney: Great. I notice, over the last month or so there's been a number of job postings from [A]pplied for various regional sales positions, I guess to start what do you think of as sort of a commercial build that's going to be necessary here to launch galactosemia and the sort of those job openings underpin a level of confidence and your potential approval?
>
> A - Shoshana Shendelman: Yes. *{FS46}* **So we do feel that the review is going well where we should be**, but we're also being thoughtful and trying to right-size our organization to where we are at that point in time. I think that's important as well. *{FS47}* **So our goal is to be prepared for the launch and to take all the necessary steps that we should be doing now** without unnecessarily burning through capital and ensuring that we have a strong cash runway which we do.
>
> *{FS48}* **And so the way that we framed this is we waited until we felt sort of an additional derisking**. The mid-cycle review meeting was completed at the end of the spring. We've currently hired in all our heads of functions for commercial. While you might see that we're maybe posting for Salesforce, we've not hired a Salesforce yet. I think like a lot of companies, will wait till a little bit closer to the approval date to get that moving.
>
> *{FS49}* **But I think we have the right level of commercial preparation happening as we move through the approval process and towards the launch**, so that we can really have a strong launch, while at the same time ensuring that we're appropriately building the organization.

231. In closing, Skorney asked Dr. Shendelman "is there anything else that I haven't asked that investors should be thoughtful of as they consider APLT?" Dr. Shendelman responded:

> *{FS50}* **I think that we're in really good shape with both programs. We're looking forward to the catalyst that we have ahead. I think it's a really**

important time for us as we hit the final stretch into approval of both of our programs. I think we're in a good place with regard to commercialization and being prepared for that big transition ahead of us from a development stage to a commercial-stage company. So I'm excited about what's ahead. I think we have a few really big things coming ahead, and we're excited.

232. FS42 through FS50 were materially false and misleading in violation of Section 10(b) and Rule 10b-5 because they contained untrue statements of material fact or omitted to state material facts necessary in order to make the statements made not misleading. Specifically, at the time these statements were made, Dr. Shendelman and Applied were aware of, or were severely reckless in not knowing, that (a) FDA regulations required the NDA to include "a description and analysis of any other data or information relevant to an evaluation of the safety and effectiveness of [govorestat] obtained or otherwise received by [Applied] from any source…including information derived from clinical investigations," (b) that the Dosing Errors and Dosing Errors Clinical Data was such "other data or information," (c) that in the NDA, Applied failed to provide the FDA with a description or analysis of the Dosing Errors or the Dosing Errors Clinical Data, and (d) that instead, as the FDA subsequently stated, "reported dose levels for subjects as stated in the protocol…rather than the actual dose levels administered."

233. Further, Defendants knew, or recklessly disregarded, that they would be, and in fact had already been, subject to an FDA investigation in connection with the NDA, and as such there was a significant risk that the Dosing Errors and Dosing Errors Clinical Data would be discovered by the FDA. As such, these undisclosed facts were negative material factors and a significant risk that the FDA would not approve the NDA because they raised significant concerns about the validity, reliability, and integrity of the clinical data and Applied's oversight and conduct of its clinical investigations.

234. FS42 through FS50 were also materially false and misleading in violation of Section 10(b) and Rule 10b-5 because, at the time these statements were made, Dr. Shendelman

and Applied were aware of, or were severely reckless in not knowing, that (a) Applied had informed the FDA that electronic source data for 11 subjects in the Pediatric Study had been deleted and not been recovered, (b) as a result, this data could not be verified by the FDA as part of its investigation, which raised concerns about the validity and integrity of the data collected during the Pediatric Study, (c) that Applied, the NDA, and Pediatric Study were in violation of 21 C.F.R. § 312.58 and the terms of the protocol for the Pediatric Study; (d) that Applied could not rectify the "objectionable condition" identified by the FDA of the deletion of the electronic clinical data for 11 test subjects; (e) that these facts, in addition to the omission of the Dosing Errors and Dosing Errors Clinical Data from the NDA, were a serious and material risk that the FDA would reject the NDA; and (f) that there existed a serious and material negative development for the Company's prospects for NDA approval and ability to commercialize govorestat.

235. By failing to disclose these material facts, Dr. Shendelman and Applied misled investors and the public, who as a result, reasonably believed that (a) the NDA complied with FDA regulations, (b) the NDA contained all required information and clinical results from the Pediatric Study, (c) the NDA accurately reported the clinical data Applied obtained for the study, (d) the FDA had not identified, and Defendants were not aware of, any issues with the NDA or the clinical data underlying the NDA, and (e) there were no known material risks to approval of the NDA, when in fact this was not true.

236. For these reasons related to the Dosing Errors and the Study Data Deletion, Dr. Shendelman and Applied did not have a reasonable basis to speak concerning positive interactions with the FDA, likelihood of approval of the NDA, or likelihood of commercialization of govorestat, especially in the near term, and had a duty to disclose all material facts concerning those subjects to ensure that a reasonable investor would not be misled.

c) Dr. Shendelman and Applied Announced a Regulatory Update on September 18, 2024 in a Press Release and at the 2024 Cantor Global Healthcare Conference, But Again Fail to Disclose the Study Data Deletion or the Form 483

237. On September 18, 2024, during pre-market hours, the Company issued a press release titled "Applied Therapeutics Provides Regulatory Update on Govorestat for the Treatment of Classic Galactosemia" (the "9/18/2024 Press Release"), announcing that the FDA had canceled the anticipated Advisory Committee Meeting:

> The Company recently completed its late-cycle review meeting with the [FDA]. The FDA communicated that an Advisory Committee meeting would no longer be required, which was previously tentatively scheduled for October 9, 2024. The FDA informed the Company that the Priority Review of the NDA is continuing as planned with alignment on post-marketing requirements expected in October 2024. The previously announced [PDUFA] target action date remains on track for November 28, 2024.
>
> *{FS51}* **We are incredibly pleased by the ongoing collaborative dialogue with the FDA during the NDA review process, and we look forward to continuing to work together with the agency to bring the first potential treatment to Classic Galactosemia patients**…Galactosemia is a progressive disease in urgent need of treatment, and *{FS52}* **the potential approval of govorestat will be transformative for the many patients and families living with this serious disease. Our commitment to the Classic Galactosemia community is further supported by our thoughtful commercial preparation, focused on establishing an effective patient access program, high physician awareness and strong payor engagement.**

238. Also, on September 18, 2024, at approximately 10:20 a.m. ET, Dr. Shendelman presented on behalf of the Company at the 2024 Cantor Global Healthcare Conference. Dr. Shendelman used a slide presentation at the 2024 Cantor Global Healthcare Conference, but that presentation has not been publicly disclosed.

239. At the 2024 Cantor Global Healthcare Conference, Dr. Shendelman characterize the cancellation of the Advisory Committee meeting as a positive development:

> As a company, we're based here in New York. We're well capitalized and I think rightsized for where we are as an organization *{FS53}* **and in the process of making that transition from clinical development stage to commercial stage company**.

In terms of our pipeline, our late-stage asset govorestat is under regulatory review right now for Classic Galactosemia in the U.S. as well as in Europe. *{FS54}* **We had some positive news this morning. So this presentation is well-timed. We recently completed our late cycle review meeting with FDA, which was very positive. They had previously communicated maybe there would be an advisory committee meeting. They let us know at the late cycle meeting that they no longer felt that was needed.** Our next interaction with them will be in about a month when we discuss post-marketing requirements. *{FS55}* **And overall, our message there is that things are going well. We're very encouraged by the dialogue with FDA and we're excited about moving forward into this last stage of regulatory review.**

* * *

{FS56} **We are at that critical transition. As I mentioned, we're in the last phase of regulatory review right now and we're preparing for a potential commercial launch. Our PDUFA date with the FDA is November 28, which is Thanksgiving Day, so we have a couple of months. We have been preparing for quite a while now. We have a strong commercial team in place and medical field team.** And I think that the key take away is that we're being thoughtful about our commercial preparation and it's rightsized to our organization. Our team members are very experienced, they've done this before in very similar rare diseases.

* * *

So to close, we have two late stage programs. *{FS57}* **Galactosemia which were in the sort of last leg of regulatory review with both the FDA and the EMA, and we're hopeful for a near term approval and launch. We're preparing diligently but thoughtfully for those commercial launches to make sure that we're set up for success, but that we remain well capitalized which is important to us. And I think we're in a very good place from a capitalization perspective.**

* * *

{FS58} **And with the potential to have two indications launched on -- and that synergy within our commercial infrastructure and sales force, I think we're very well set up for the future to be successful as a rare disease company and also to do something really meaningful for patients with these disease**s. Again, there's just a huge unmet medical need in both Galactosemia and SORD Deficiency. And so we have an opportunity to bring something to those patients indeed, which I think is what gets us all out of bed in the morning. So thank you very much for your time.

240. FS51 through FS58 were materially false and misleading in violation of Section 10(b) and Rule 10b-5 because they contained untrue statements of material fact or omitted to state

material facts necessary in order to make the statements made not misleading. Specifically, at the time these statements were made, Dr. Shendelman and Applied were aware of, or were severely reckless in not knowing, that (a) FDA regulations required the NDA to include "a description and analysis of any other data or information relevant to an evaluation of the safety and effectiveness of [govorestat] obtained or otherwise received by [Applied] from any source…including information derived from clinical investigations," (b) that the Dosing Errors and Dosing Errors Clinical Data was such "other data or information," (c) that in the NDA, Applied failed to provide the FDA with a description or analysis of the Dosing Errors or the Dosing Errors Clinical Data, and (d) that instead, as the FDA subsequently stated, "reported dose levels for subjects as stated in the protocol…rather than the actual dose levels administered."

241. Further, Defendants knew, or recklessly disregarded, that they would be, and in fact had already been, subject to an FDA investigation in connection with the NDA, and as such there was a significant risk that the Dosing Errors and Dosing Errors Clinical Data would be discovered by the FDA. As such, these undisclosed facts were negative material factors and a significant risk that the FDA would not approve the NDA because they raised significant concerns about the validity, reliability, and integrity of the clinical data and Applied's oversight and conduct of its clinical investigations.

242. FS51 through FS58 were also materially false and misleading in violation of Section 10(b) and Rule 10b-5 because, at the time these statements were made, Dr. Shendelman and Applied were aware of, or were severely reckless in not knowing, that (a) Applied had informed the FDA that electronic source data for 11 subjects in the Pediatric Study had been deleted and not been recovered, (b) as a result, this data could not be verified by the FDA as part of its investigation, which raised concerns about the validity and integrity of the data collected

during the Pediatric Study, (c) that Applied, the NDA, and Pediatric Study were in violation of 21 C.F.R. § 312.58 and the terms of the protocol for the Pediatric Study; (d) that Applied could not rectify the "objectionable condition" identified by the FDA of the deletion of the electronic clinical data for 11 test subjects; (e) that these facts, in addition to the omission of the Dosing Errors and Dosing Errors Clinical Data from the NDA, were a serious and material risk that the FDA would reject the NDA; and (f) that there existed a serious and material negative development for the Company's prospects for NDA approval and ability to commercialize govorestat.

243. By failing to disclose these material facts, Dr. Shendelman and Applied misled investors and the public, who as a result, reasonably believed that (a) the NDA complied with FDA regulations, (b) the NDA contained all required information and clinical results from the Pediatric Study, (c) the NDA accurately reported the clinical data Applied obtained for the study, (d) the FDA had not identified, and Defendants were not aware of, any issues with the NDA or the clinical data underlying the NDA, and (e) there were no known material risks to approval of the NDA, when in fact this was not true.

244. For these reasons related to the Dosing Errors and the Study Data Deletion, Dr. Shendelman and Applied did not have a reasonable basis to speak concerning the positive nature of the cancellation of the Advisory Committee meeting, the likelihood of approval of the NDA, commercialization of govorestat, or positive communications with the FDA, and once they chose to speak concerning these topics, had a duty to disclose all material facts concerning those subjects to ensure that a reasonable investor would not be misled.

245. Further, by providing a regulatory update, but not mentioning all relevant information, including the Form 483 or the Study Data Deletion, and characterizing the regulatory update as a positive development, the Defendants misled investors and the public into thinking

there were no other known regulatory developments or negative factors impacting potential approval of the NDA and that approval of the NDA was even more likely to occur.

246. The conclusion that FS51 through FS58 were materially false and misleading is further supported by the fact that, in the 9/18/2024 Press Release and FS54, Dr. Shendelman mentioned "the last cycle review meeting with the FDA," which she described as "very positive" in FS54. However, Dr. Shendelman failed to disclose that, on September 5, and 11, 2024, as part of the background package for that late cycle review meeting, Applied and the FDA engaged in written correspondence concerning the Study Data Deletion, and Applied re-affirmed that it could not recover the electronic source data for 11 patients in the Pediatric Study. Therefore, as part of the late cycle meeting, Applied discussed with the FDA facts that evidenced a significant material risk that the NDA would not be approved, which would, at a minimum, be a fact that needed to be disclosed to ensure investors had the full picture of the "very positive" meeting and cancellation of the Advisory Committee meeting.

247. Investors reacted favorably to Dr. Shendelman's and Applied's September 18 statements, and the price of Applied Therapeutics common stock skyrocketed. On September 18, 2024, the price of Applied common stock increased $3.20 per share, or 68.9%, from a closing price of $4.65 per share on September 17, 2024, to a closing price of $7.85 per share on September 18, 2024, on volume of more than 51.6 million shares, more than 40 times the trading volume of Applied common stock on the previous trading day.

248. Analysts also reacted favorably to the news that the Advisory Committee meeting for the NDA was cancelled. On September 18, 2024, Leerink analyst Joseph Schwartz stated "we think this is very good news" and that its "not surprising to us since we have been looking at the totality of the data since our initiation." Schwartz also added "The majority of clinical outcomes

that would have been included in the original primary endpoint favored govorestat…and only grew stronger when APLT updated their cognition data after calculations errors made by a vendor were discovered."

d) The 11/6/2024 Pediatric Study Results Contained Materially False and Misleading Statements Concerning the Clinical Data in the Study

249. On November 6, 2024, the11/6/2024 Pediatric Study Results were published in *The Journal of Clinical Pharmacology*. The 11/6/2024 Pediatric Study Results were also published to Applied's website.

250. The 11/6/2024 Pediatric Study Results (in entirety, *{FS59}*) were materially false and misleading in violation of Section 10(b) and Rule 10b-5 at the time it was published because it contained untrue statements of fact or omitted to state material facts necessary in order to make the statements made, in the light of the circumstances under which they were made, not misleading. Specifically, the 11/6/2024 Pediatric Study Results discussed the dosages given to clinical patients and the clinical results of the study. For example, the 11/6/2024 Study Results stated (at 5):

> dosing was converted to weight-based dosing for the long-term clinical outcomes portion of the study with children weighing under 20 kg dosed at 30 mg/kg; children weighing 20 to 40 kg dosed at 20 mg/kg; and children weighing over 40 kg dosed at 15 mg/kg… At the doses outlined above, participants achieved a uniform exposure with a Cmax of 44.01 µg/mL (geometric percent coefficient of variation [GeoCV%] of 45.28) and AUCtau of 381.89 µg*h/mL (GeoCV% of 45.61) with a time to maximal concentration (Tmax) of 4 h after dosing.

251. Further results concerning Pharmacodynamic Biomarker Effects, Clinical Outcomes, Clinical Meaningfulness of Change, Safety, followed on pages 5 through 11 of the 11/6/2024 Study Results

252. However, the 11/6/2024 Study Results made no mention of the Dosing Errors or the Dosing Errors Clinical Data. At the time the 11/6/2024 Study was submitted for publication and published, Dr. Shendelman, Dr. Perfetti, and Applied knew that there were additional clinical

results for the Pediatric Study that were not disclosed in FS59 or the NDA, namely the Dosing Errors Clinical Data. Reasonable investors would conclude that the results included in the 9/4/2024 Presentation were the same results that were used to support the NDA. By failing to disclose the Dosing Errors or the Dosing Errors Clinical Data, Defendants led investors to believe that the results described above were the complete results of the Pediatric Study, and there were no other results from the study that were required to be included in the NDA. Defendants further led investors to believe that the clinical data in the 11/6/2024 Study Results was verifiable, when in fact it was not due to the Study Data Deletion.

e) Defendants' November 7, 2024 Press Release, Form 8-K, and Form 10-Q Concerning Applied's Third Quarter 2024 Financial Results Contained Materially False and Misleading Statements Regarding the NDA and Commercialization of Govorestat

253. On November 7, 2024, during pre-market hours, the Company issued a press release titled "Applied Therapeutics Reports Third Quarter 2024 Financial Results" (the 11/7/2024 Press Release"). Also on November 7, 2024, during pre-market hours, the Company filed a Form 8-K with the SEC that attached the 11/7/2024 Press Release as an exhibit (the "11/7/2024 Form 8-K"). The 11/7/2024 Form 8-K was signed by Dr. Shendelman.

254. In addition, on November 7, 2024, during pre-market hours, the Company filed its Form 10-Q for the third fiscal quarter of 2024 ending September 30, 2024 with the SEC (the "3Q 2024 Form 10-Q"). The 3Q 2024 Form 10-Q was signed by Dr. Shendelman and Mr. Funtleyder.

255. The 11/7/2024 Press Release restated FS3, a statement substantially similar to FS1, and the 3Q 2024 Form 10-Q restated FS1, which were false and misleading for the reasons stated in paragraphs 80-82.

> *{FS3}* **The [NDA] submission package included clinical outcomes data from the Phase 3 registrational ACTION-Galactosemia Kids study in children aged 2-17 with Galactosemia, the Phase 1/2 ACTION-Galactosemia study in adult patients with Galactosemia, and preclinical data.**

{FS1} **The NDA and MAA submission packages include clinical outcomes data from the Phase 3 registrational ACTION-Galactosemia Kids study in children age[d] 2-17 with Galactosemia, the Phase 1/2 ACTION-Galactosemia study in adult patients with Galactosemia, and preclinical data**.

256. The 3Q 2024 Form 10-Q also restated FS36, which was false and misleading for the reasons stated in paragraph 197 and 199-203:

{FS36} In the second quarter of 2024, **in the process of preparing for FDA inspection, it was discovered that the vendor we engaged to compile NIH Toolbox data for the Company used an adult formula for calculation of about one third of composite cognition and motor skills scores. Adjusting the formula to the pediatric formula resulted in significantly improved data for cognition as compared to the prior data, demonstrating improvement in the govorestat treated group of approximately 8 points on a standard scale, which was statistically significant compared to placebo (p=0.032). This also resulted in a statistically significant effect on the primary endpoint sensitivity analysis which included cognition (p=0.034). The motor skills data did not change substantially. These updates were disclosed and discussed with the FDA and EMA and will be used in the ongoing evaluation of the NDA and MAA.**

257. The 3Q 2024 Form 10-Q (at 49) also restated the risk factor FS19 from the 1Q 2024 Form 10-Q, which was false and misleading for the reasons stated in paragraph 165:

Prior to obtaining approval to commercialize any product candidate in the United States or abroad, *{FS19}* **we must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA or comparable foreign regulatory authorities, that such product candidate is safe and effective for its intended uses.**

258. Dr. Shendelman was quoted in the 11/7/2024 Press Release as stating:

{FS60} **We are proud of the significant progress we've made this quarter as we prepare for a transformational year ahead, with a focus on transitioning from a clinical-stage company to a commercial organization. With regulatory submissions for govorestat underway in two rare disease indications of urgent unmet need, Classic Galactosemia and SORD Deficiency, we continue to thoughtfully execute our pre-launch initiatives** …

*{FS61}***As we approach the final stages of the NDA review process for Classic Galactosemia in parallel with a near-term NDA submission for SORD Deficiency, we remain confident in the promise of govorestat and its ability to address the underlying mechanisms of both diseases. We look forward to the opportunity to bring govorestat to patients in 2025.**

259. FS60 and FS61 were materially false and misleading in violation of Section 10(b) and Rule 10b-5 because they contained untrue statements of material fact or omitted to state material facts necessary in order to make the statements made not misleading. Specifically, at the time these statements were made, Dr. Shendelman and Applied were aware of, or were severely reckless in not knowing, that (a) FDA regulations required the NDA to include "a description and analysis of any other data or information relevant to an evaluation of the safety and effectiveness of [govorestat] obtained or otherwise received by [Applied] from any source…including information derived from clinical investigations," (b) that the Dosing Errors and Dosing Errors Clinical Data was such "other data or information," (c) that in the NDA, Applied failed to provide the FDA with a description or analysis of the Dosing Errors or the Dosing Errors Clinical Data, and (d) that instead, as the FDA subsequently stated, "reported dose levels for subjects as stated in the protocol…rather than the actual dose levels administered."

260. Further, Defendants knew, or recklessly disregarded, that they would be, and in fact had already been, subject to an FDA investigation in connection with the NDA, and as such there was a significant risk that the Dosing Errors and Dosing Errors Clinical Data would be discovered by the FDA. As such, these undisclosed facts were negative material factors and a significant risk that the FDA would not approve the NDA because they raised significant concerns about the validity, reliability, and integrity of the clinical data and Applied's oversight and conduct of its clinical investigations.

261. FS60 and FS61 were also materially false and misleading in violation of Section 10(b) and Rule 10b-5 because, at the time these statements were made, Dr. Shendelman and Applied were aware of, or were severely reckless in not knowing, that (a) Applied had informed the FDA that electronic source data for 11 subjects in the Pediatric Study had been deleted and not

been recovered, (b) as a result, this data could not be verified by the FDA as part of its investigation, which raised concerns about the validity and integrity of the data collected during the Pediatric Study, (c) that Applied, the NDA, and Pediatric Study were in violation of 21 C.F.R. § 312.58 and the terms of the protocol for the Pediatric Study; (d) that Applied could not rectify the "objectionable condition" identified by the FDA of the deletion of the electronic clinical data for 11 test subjects; (e) that these facts, in addition to the omission of the Dosing Errors and Dosing Errors Clinical Data from the NDA, were a serious and material risk that the FDA would reject the NDA; and (f) that there existed a serious and material negative development for the Company's prospects for NDA approval and ability to commercialize govorestat.

262. By failing to disclose these material facts, Dr. Shendelman and Applied misled investors and the public, who as a result, reasonably believed that (a) the NDA complied with FDA regulations, (b) the NDA contained all required information and clinical results from the Pediatric Study, (c) the NDA accurately reported the clinical data Applied obtained for the study, (d) the FDA had not identified, and Defendants were not aware of, any issues with the NDA or the clinical data underlying the NDA, and (e) there were no known material risks to approval of the NDA, when in fact this was not true.

263. For these reasons related to the Dosing Errors and the Study Data Deletion, Dr. Shendelman and Applied did not have a reasonable basis to speak concerning regulatory progress, the likelihood of approval of the NDA, likelihood of commercialization of govorestat, or transition to a commercial stage company, and once they chose to speak concerning the NDA and these topics, had a duty to disclose all material facts concerning those subjects to ensure that a reasonable investor would not be misled.

264. Attached to the 3Q 2024 Form 10-Q as Exhibit 31.1 was a signed certification, dated August 7, 2024, by Dr. Shendelman pursuant to the Sarbanes Oxley Act stating:

> I have reviewed this Form 10-Q of Applied Therapeutics, Inc.;
>
> *{FS62}* **Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report**.

265. FS62 was materially false and misleading in violation of Section 10(b) and Rule 10b-5 because it was an untrue statement of fact. Dr. Shendelman knew that FS1, FS19, FS36 were included in the 3Q 2024 Form 10-Q and were materially false and misleading.

f) Dr. Shendelman's November 12, 2024 Presentation at the UBS Global Healthcare Conference Contained Materially False and Misleading Statements Concerning the NDA and Commercialization of Govorestat

266. On November 12, 2024, at approximately 10:15 a.m. ET, Dr. Shendelman, on behalf of the Company, presented at the 2024 UBS Global Healthcare Conference. Dr. Shendelman used a slide presentation, but that presentation has not been publicly disclosed. At the conference, Dr. Shendelman stated:

> At Applied Therapeutics, we're developing drugs for rare diseases and specifically we're targeting rare diseases that have no treatment options available. *{FS63}* **We have a very late stage asset that's under regulatory review for one indication, classic Galactosemia and we're preparing for a regulatory submission for the second indication called SORD Deficiency. Both of these indications have the potential for near term commercial launches**, and we're well capitalized to bring us through these milestones. I'll talk in a little bit more detail about what these rare diseases are, but Galactosemia and SORD Deficiency are both rare diseases that involve sugar metabolism. And govorestat previously called AT-007 is a central nervous system penetrant oral Aldose Reductase inhibitor that we've developed for both of these indications. *{FS64}* **And again it's currently under regulatory review in the U.S. and Europe for the treatment of classic Galactosemia. You'll note that our PDUFA date in the U.S. is November 28th, which is just a few weeks away and we're simultaneously under review in Europe and we're expecting a CHMP [Committee for Medicinal Products for Human Use] opinion in the first quarter of '25….**

{FS65} **And again, they're in the very late stages of regulatory review** and submission soon for SORD Deficiency…

{FS66} **And I'm sure everyone has noted our PDUFA date is right around the corner. So we have been preparing for commercial launch. We've taken steps that I think are appropriate, building a right sized and experienced commercial team**. Every step along the way we've been driving disease awareness and education both amongst the physician community and the patient and caregiver community. We've been very engaged with physicians and payers. And again as mentioned, this is all of the commercial infrastructure that we've built for Galactosemia can also be leveraged for SORD Deficiency. We've also built extensive patient support and access services for the Galactosemia community, which again will also be meaningful for the SORD community when we get there…

{FS67} **So to sum up, govorestat is in late stage review and development for two rare diseases, Galactosemia and SORD Deficiency**. These are both rare diseases with high urgent unmet medical need. They're devastating progressive diseases with no treatments approved. So there's an opportunity for govorestat to really be life changing for these patients and to offer the first potential opportunity for treatment for both of these diseases. *{FS68}* **For Galactosemia, we're under review at the FDA with a PDUFA date of November 28th this month** and our MAA is under review in Europe again expecting a CHMP decision in the first quarter of '25. With SORD Deficiency, we are planning to submit our NDA in the first quarter of '25. *{FS69}* **So we have the potential to have two launches in very close proximity to one another and we've spent a lot of this year preparing for that. So I think we're very well prepared, we're in a good place to successfully launch in both of these indications and we're excited about the evolution of the company at this important time as we go from clinical stage to potentially commercial stage**. Thank you everyone for your attention. I'm sorry that we can't do a Q&A at this presentation, but thank you.

267. FS63 through FS69 were materially false and misleading in violation of Section 10(b) and Rule 10b-5 because they contained untrue statements of material fact or omitted to state material facts necessary in order to make the statements made not misleading. Specifically, at the time these statements were made, Dr. Shendelman and Applied were aware of, or were severely reckless in not knowing, that (a) FDA regulations required the NDA to include "a description and analysis of any other data or information relevant to an evaluation of the safety and effectiveness of [govorestat] obtained or otherwise received by [Applied] from any source…including information derived from clinical investigations," (b) that the Dosing Errors and Dosing Errors

Clinical Data was such "other data or information," (c) that in the NDA, Applied failed to provide the FDA with a description or analysis of the Dosing Errors or the Dosing Errors Clinical Data, and (d) that instead, as the FDA subsequently stated, "reported dose levels for subjects as stated in the protocol…rather than the actual dose levels administered."

268. Further, Defendants knew, or recklessly disregarded, that they would be, and in fact had already been, subject to an FDA investigation in connection with the NDA, and as such there was a significant risk that the Dosing Errors and Dosing Errors Clinical Data would be discovered by the FDA. As such, these undisclosed facts were negative material factors and a significant risk that the FDA would not approve the NDA because they raised significant concerns about the validity, reliability, and integrity of the clinical data and Applied's oversight and conduct of its clinical investigations.

269. FS63 through FS69 were also materially false and misleading in violation of Section 10(b) and Rule 10b-5 because, at the time these statements were made, Dr. Shendelman and Applied were aware of, or were severely reckless in not knowing, that (a) Applied had informed the FDA that electronic source data for 11 subjects in the Pediatric Study had been deleted and not been recovered, (b) as a result, this data could not be verified by the FDA as part of its investigation, which raised concerns about the validity and integrity of the data collected during the Pediatric Study, (c) that Applied, the NDA, and Pediatric Study were in violation of 21 C.F.R. § 312.58 and the terms of the protocol for the Pediatric Study; (d) that Applied could not rectify the "objectionable condition" identified by the FDA of the deletion of the electronic clinical data for 11 test subjects; (e) that these facts, in addition to the omission of the Dosing Errors and Dosing Errors Clinical Data from the NDA, were a serious and material risk that the FDA would

reject the NDA; and (f) that there existed a serious and material negative development for the Company's prospects for NDA approval and ability to commercialize govorestat.

270. By failing to disclose these material facts, Dr. Shendelman and Applied misled investors and the public, who as a result, reasonably believed that (a) the NDA complied with FDA regulations, (b) the NDA contained all required information and clinical results from the Pediatric Study, (c) the NDA accurately reported the clinical data Applied obtained for the study, (d) the FDA had not identified, and Defendants were not aware of, any issues with the NDA or the clinical data underlying the NDA, and (e) there were no known material risks to approval of the NDA, when in fact this was not true.

271. For these reasons related to the Dosing Errors and the Study Data Deletion, Dr. Shendelman and Applied did not have a reasonable basis to speak concerning the likelihood of approval of the NDA or the commercial launch of govorestat, and once they chose to speak concerning the NDA and these topics, had a duty to disclose all material facts concerning those subjects to ensure that a reasonable investor would not be misled.

272. Dr. Shendelman's statements led the market to believe that approval of the NDA was imminent. On November 27, 2024, the day the CRL and Warning Letter were received by Applied and Dr. Shendelman, and before any disclosure of the CRL or Warning Letter was made, Citigroup Global Markets issued an analyst note concerning Applied Therapeutics, which stated Citigroup saw an "85%" chance of approval of the NDA and raised its price target for Applied common stock from $11 per share to $13 per share:

> We currently have a positive catalyst watch for the approval of govorestat in galactosemia and continue to see an 85% PoS. Assuming the potential FDA approval this week leading to initial revenue production in 2025 by our forecasts, plus the option to monetize the associated PRV, we believe the company could reach cash flow breakeven in 2026. We are raising our TP to $13 (from $11) after lowering the WACC given our high conviction on the FDA approval.

273. This report, issued the day the CRL was received by the Company, evidences how the Defendants' false and misleading statements led investors and analysts to believe that approval of the NDA and commercialization of govorestat for Classic Galactosemia was a formality, when in truth, the Defendants knew of significant and serious undisclosed negative factors and risks weighing against approval of the NDA.

B. The Truth Concerning the Defendants' False and Misleading Statements is Disclosed, Causing a Significant Decline in the Price of Company Common Stock

1. Defendants Disclose the Complete Response Letter on November 27, 2024, Causing Applied's Common Stock to Fall Significantly, But Fail to Disclose They Also Received the Warning Letter on November 27, 2024

274. On November 27, 2024, during post-market hours, the Company issued a press release titled "Applied Therapeutics Receives Complete Response Letter from U.S. FDA Regarding New Drug Application for Govorestat for Classic Galactosemia" (the "11/27/2024 Press Release") that stated:

> NEW YORK, Nov. 27, 2024 (GLOBE NEWSWIRE) -- Applied Therapeutics, Inc. (Nasdaq: APLT), a biopharmaceutical company dedicated to creating transformative treatments for rare disease, today announced that the U.S. Food and Drug Administration (FDA) has issued a Complete Response Letter (CRL) for the New Drug Application (NDA) for govorestat, a novel, central nervous system (CNS)-penetrant aldose reductase inhibitor (ARI), for the treatment of Classic Galactosemia.
>
> The CRL indicates that the FDA completed its review of the application and determined that it is unable to approve the NDA in its current form, citing deficiencies in the clinical application.
>
> Applied Therapeutics is reviewing the feedback from the FDA and plans to immediately request a meeting to discuss requirements for a potential resubmission of the NDA or appeal of the decision along with appropriate next steps.
>
> "We are disappointed by the FDA's decision today. Our strong commitment to the Galactosemia community is rooted in our belief that govorestat has the potential to change the lives of patients with Galactosemia, which we believe is evidenced by the breadth of efficacy and safety data demonstrating its ability to stop the decline on progressive clinical outcomes, including cognition and behavior," said Shoshana Shendelman, PhD, Founder and CEO of Applied Therapeutics. "Galactosemia is a

> progressive and debilitating disease without any existing treatment options and there remains a high unmet medical need for this community. As we move forward, we plan to work with the FDA to address the concerns in the CRL and determine an expeditious path to bring this much needed treatment to patients. We are grateful to the patients, families, and healthcare providers who participated in the govorestat clinical studies."

275. Also on November 27, 2024, after market hours, the Company filed a Form 8-K with the SEC that disclosed the receipt of the CRL (the "11/27/2024 Form 8-K"). The 11/27/2024 Form 8-K was signed by Dr. Shendelman.

> On November 27, 2024, Applied Therapeutics, Inc. (the "Company") announced that the U.S. Food and Drug Administration ("FDA") has issued a Complete Response Letter ("CRL") for the New Drug Application ("NDA") for govorestat, a novel, central nervous system ("CNS")-penetrant aldose reductase inhibitor ("ARI"), for the treatment of Classic Galactosemia.
>
> The CRL indicates that the FDA completed its review of the application and determined that it is unable to approve the NDA in its current form, citing deficiencies in the clinical application.
>
> The Company is reviewing the feedback from the FDA and plans to immediately request a meeting to discuss requirements for a potential resubmission of the NDA or appeal of the decision along with appropriate next steps.

276. However, unknown to investors, also on November 27, 2024, Dr. Shendelman and Applied received the Warning Letter by email. The Warning Letter was signed by David C. Burrow, Pharm.D., J.D., Director, Office of Scientific Investigations, Office of Compliance, Center for Drug Evaluation and Research, U.S. Food and Drug Administration, at 9:09:23 a.m. There is therefore a strong inference that Dr. Shendelman received the Warning Letter in the morning of November 27, 2024.

277. Applied would not disclose the existence of the Warning Letter for five more days, on December 2, 2024. As a result, the *{FS70}* 11/27/2024 Press Release and *{FS71}* 11/27/2024 Form 8-K were materially false and misleading in violation of Section 10(b) and Rule 10b-5 because they omitted material facts that the Defendants had a duty to disclose in order to make the

statements made by Defendants, in light of the circumstances under which they were made, not misleading, namely that the Defendants received the Warning Letter and the contents of the Warning Letter. Further, once Defendants chose to disclose information about the FDA's denial of the NDA, they had an obligation to disclose all material facts.

278. Research analysts were surprised by the CRL, and concluded that the CRL was a significant negative development for Applied. On November 29, 2024, William Blair published a report that described the CRL as "a Major Setback" and that stated the following: "[a]fter speaking with management, it noted that the FDA had not provided enough information on the reason for the CRL, but suspects it was related to the efficacy package as opposed to CMC [chemistry, manufacturing, and controls] or safety." The analyst also noted: "Management also shared that leading into the PDUFA, communication with the FDA during the review cycle was productive and discussion of the primary endpoint in the study not reaching statistical significance was exhaustive." In response, William Blair lowered the "probability of success for the galactosemia program to 30%."

279. On November 29, 2024, Leerink Partners published a report that stated that the CRL "comes as a major surprise, given the progress the company appeared to be making with the FDA" and "[w]e thought the FDA review had been progressing favorably based on the information available to us."

280. Also on November 29, 2024, RBC Capital Markets published a report that stated that "[t]he CRL for govorestat in galactosemia is disappointing, and we believe creates significant uncertainties around a future path forward for the drug in that indication." Notably, the analysts thought that "next steps would likely require another clinical trial, pushing back galactosemia timelines meaningfully and adding considerable risk." This caused RBC Capital Markets to lower

its price target for Applied common stock from $12 to $4 per share, reduce its rating to sector perform from outperform, and adjust the probability of success for the NDA to 20%, from 70%. Also, RBC Health of Global Healthcare Research Brian Adams said in his research note that "we had thought the drug was more likely than not to be approve," evidencing how the Defendants' materially misleading statements misled the market to the true state of affairs. Further, Abrahams stated that "the primary endpoint mis had always posed a risk [and] there were a number of complexities in the data," evidencing that the market had no warning of the serious regulatory issues at Applied that led to the CRL and the Warning Letter.

281. On November 29, 2024, research analyst William Blair reacted to the CRL, stating that it was "unexpected and disappointing," as well as a "major setback." As alleged above, prior to this, William Blair had anticipated the NDA would be approved.

282. Also on November 29, 2024, research analyst Citigroup lowered its price target for Applied common stock from $13 per share to $8 per share. The Citigroup analyst also attributed the CRL to "the missed primary endpoint." Research analyst Baird lowered its price target for Applied common stock from $14 per share to $5 per share, and analyst Brian Skorney stated that the "credibility damage will be touch to bounce back from following the FDA's Thanksgiving rejection in galactosemia and lack of substantial detail around how the review went south."

283. In response to the disclosure of the CRL and rejection of the NDA, the price of Applied common stock declined $6.54 per share, or 76.3%, on Friday November 29, 2024 (the next trading day), from a closing price of $8.57 per share on November 27, 2024 to a closing price of $2.03 per share on November 29, 2024, on extremely high volume of 43.9 million shares, more than 23 times the average trading volume of Applied common stock from the start of the Class Period through November 27, 2024.

284. November 29, 2024 was the day after the Thanksgiving Holiday, and the NASDAQ market closed for trading on November 29, 2024 early at 1:00 p.m. ET.

285. On December 2, 2024, UBS Securities issued a report on Applied, which downgraded Applied from Buy to Neutral, reduced the price target for Applied from $13 per share to $2 per share, and stated that "[w]e think unknowns around the deficiencies resulting in the [FDA's complete response letter] create uncertainty for the shares" and "[w]e model 25% and 35% probability of success to approval for govorestat in galactosemia and SORD, respectively. Although galactosemia and SORD are rare conditions where we see a high unmet need (no approved therapies), we see uncertainties around the regulatory path forward from here."

286. Also on December 2, 2024, Baird issued an analyst report on Applied that lowered the price target for Applied common stock to $5 per share from $14 per share.

287. The price of Applied Therapeutics common stock continued its decline in response to the disclosure of the CRL and rejection of the NDA on Monday December 2, 2024, closing at $1.75 per share, an additional decline of $0.28 per share, on volume of 29.9 million shares, nearly 16 times the average trading volume of Applied common stock from the start of the Class Period through November 27, 2024.

2. Defendants and the FDA Disclose the Warning Letter on December 2 and 3, 2024, Causing Applied's Stock to Further Decline

288. On December 2, 2024, after market close, Applied filed a Form 8-K disclosing the existence of the Warning Letter (the "12/2/2024 Form 8-K"). The 12/2/2024 Form 8-K was signed by Dr. Shendelman. The filing stated that the FDA inspection had focused on the Pediatric Study and referenced issues concerning deleted electronic data and dosing deviations.

> In the normal course of Applied Therapeutics, Inc.'s (the "Company") New Drug Application ("NDA") review for govorestat, the U.S. Food and Drug Administration ("FDA") performed an inspection relating to the AT-007-1002 study. The Company responded to the FDA's inspectional observations and

> believed it addressed any outstanding questions or issues. Following issuance of a Complete Response Letter ("CRL"), the Company received a warning letter limited to the AT-007-1002 study. The letter identified issues related to electronic data capture, which the Company believes were addressed in prior communications with the agency, including by providing detailed paper and video records. The letter also refers to a dosing error in the dose-escalation phase of the study resulting in slightly lower levels than targeted in a limited number of patients, which was remedied prior to achieving maintenance dosing. Detailed records were maintained by the Company under FDA regulatory requirements, and this information was provided to FDA. The Company intends to respond within the permitted 15 business days to address these issues.

289. Notably, the Defendants' statement that the FDA had given "inspectional observations" was misleading, as the Form 483's purpose is to identify "objectionable conditions."

290. Then on December 3, 2024, during market hours at approximately 1:30 p.m. ET, the FDA posted a copy of the Warning Letter to the FDA website. According to the Warning Letter, the Dosing Issue and the Study Data Deletion "raise[d] significant concerns about the validity and reliability of data collected for this clinical investigation." The Warning Letter stated, in full as follows (emphasis added except where noted):

> WARNING LETTER
> Applied Therapeutics, Inc.
> MARCS-CMS 696833 — December 03, 2024
>
> ---
>
> Delivery Method: VIA UNITED PARCEL SERVICE AND VIA E-MAIL
> Reference #: 24-HFD-45-11-01
> Product: Drugs
>
> ---
>
> **WARNING LETTER** 24-HFD-45-11-01
>
> November 27, 2024
>
> Dear Dr. Shendelman:
>
> This Warning Letter informs you of objectionable conditions observed during the U.S. Food and Drug Administration (FDA) inspection conducted between April 29 and May 3, 2024. Investigators Kerun Hardeo, Benton M. Ketron, and Cheryl A. Grandinetti, representing FDA, reviewed the role of Applied Therapeutics, Inc. (Applied Therapeutics) as the sponsor of a clinical investigation (Protocol [**redacted**].

This inspection was conducted as a part of FDA's Bioresearch Monitoring Program, which includes inspections designed to evaluate the conduct of research and to help ensure that the rights, safety, and welfare of human subjects have been protected.

At the conclusion of the inspection, Investigators Hardeo, Ketron, and Grandinetti discussed with you significant findings and presented the Form FDA 483, Inspectional Observations. We acknowledge receipt of your May 9, 2024, written response to the Form FDA 483.

From our review of the FDA Establishment Inspection Report, the documents submitted with that report, and your written response dated May 9, 2024, it appears that **Applied Therapeutics did not adhere to the applicable statutory requirements in the Federal Food, Drug and Cosmetic Act (FD&C Act) and applicable regulations contained in Title 21 of the Code of Federal Regulations, part 312 (21 CFR 312) governing the conduct of clinical investigations**. We wish to emphasize the following:

1. Failure to permit an authorized officer or employee of the Food and Drug Administration to have access to and copy and verify records and reports relating to the conduct of a clinical investigation [21 CFR 312.58]. [(emphasis in original).]

FDA regulations require sponsors, upon request from an authorized officer or employee of the FDA, at reasonable times, to permit such an officer or employee to have access to and copy and verify any records and reports relating to a clinical investigation. Applied Therapeutics failed to adhere to these requirements.

Specifically, for Protocol [**redacted**], Applied Therapeutics used Pearson's Q-global®, a Web-based administration system for capturing data for certain electronic clinical outcome assessments (eCOAs) performed for measuring primary and secondary efficacy endpoints. These eCOAs included the [**redacted**].

FDA requested access to verify electronic data collected and maintained in Q-global® during this inspection and during an earlier inspection conducted at one of the [**redacted**] clinical sites, Site [**redacted**] between [**redacted**] and [**redacted**].

However, on March 27, 2024, two days after FDA preannounced its inspection of one of the clinical sites, Site [redacted], a third-party vendor contracted by Applied Therapeutics deleted electronic data in Q-global®, including associated audit trails, for the [redacted] for all 47 subjects enrolled in the study at all [redacted] clinical sites. As a result, during the sponsor inspection, FDA was unable to access and copy and verify records and reports relating to the study conducted under Protocol [redacted] specifically certain electronic data collected and maintained in Q-global® for critical eCOAs for all 47 subjects at multiple study timepoints for this clinical investigation.

We acknowledge that this finding, as included on the Form FDA 483 you received, was limited to the deletion of [**redacted**] source data for 11 subjects at Site [**redacted**] and therefore your written response to the Form FDA 483 does not directly address the extent of this finding as discussed in this letter.

In your May 9, 2024, written response, you stated that the deleted [redacted] source data for 11 subjects, which was captured directly into Q-global®, could not be recovered in electronic format. You also indicated that steps have been taken to ensure the integrity of the remaining data. For example, you stated that you instructed [**redacted**] (the developers of [**redacted**] to block any further actions regarding data for this study, such that no further data could be deleted. You also stated that [**redacted**] transferred a copy of the remainder of the electronic dataset to Applied Therapeutics for backups, and the data is now warehoused with both [**redacted**] and Applied Therapeutics. In addition, you performed an assessment of systems to ensure that the third-party vendor did not have the capability to delete data from any other systems.

You further stated in your May 9, 2024, written response that preventive actions will be taken, including but not limited to the following:

1. For any new trial, Applied Therapeutics will create a data process map that clearly shows the flow and storage of collected data, to ensure that source data is maintained at both the site and at the sponsor.

2. Original paper source documents will remain at the clinical site, with a PDF copy available at the sponsor.

3. Electronic data (even if held on third-party systems) will be backed up appropriately and held at the sponsor.

4. External vendors will not have the ability to delete files from any electronic systems.

5. Appropriate electronic audit trails will be maintained such that any changes to electronic data will be identifiable and auditable.

FDA acknowledges that, in an August 27, 2024, written response to FDA's August 20, 2024, Information Request, Applied Therapeutics stated that an export of the [**redacted**] data from the backup Q-global® system is maintained with a third-party statistical consulting vendor; however, the data is no longer available in Q-global®.

FDA also acknowledges that, in a September 11, 2024, written response to FDA's September 5, 2024, correspondence providing the Late Cycle Meeting Background Package, Applied Therapeutics stated that the third-party vendor deleted the data [**redacted**] from the Q-global® system without consulting Applied Therapeutics, the sponsor. **Applied Therapeutics also stated that it was able to recover this data from the Q-global® system's backup, except for the 11** [**redacted**] **tests**.

Applied Therapeutics noted that, before the electronic data's deletion, item-level responses were captured in PDF and in paper copies of the score reports.

While we acknowledge Applied Therapeutics' response, as well as the corrective and preventive actions that Applied Therapeutics has taken and plans to take, **your response is inadequate because you did not include sufficient details about your corrective action plan. For example, you did not provide sufficient details regarding the procedures being implemented to prevent similar violations in the future. Additionally, we remain concerned that electronic data collected for critical eCOAs was deleted and cannot be verified, which raises concerns about the validity and integrity of the data collected during the clinical investigation. Without access to the pertinent electronic data in Q-global®, including associated audit trails, FDA cannot verify the accuracy, consistency, and completeness of study data collected for critical eCOAs used to measure primary and secondary efficacy endpoints, and cannot evaluate the extent and impact of any reported data errors and discrepancies. FDA also cannot confirm whether the clinical investigation was conducted in compliance with the regulatory responsibilities set forth in 21 CFR 312.**

2. Failure to provide FDA [with] a description and analysis of any other data or information relevant to an evaluation of the safety and effectiveness of the drug product obtained or otherwise received by the applicant from any source, foreign or domestic, including information derived from clinical investigations, including controlled and uncontrolled studies of uses of the drug other than those proposed in the application, commercial marketing experience, reports in the scientific literature, and unpublished scientific papers [21 CFR 314.50(d)(5)(iv)]. [(emphasis in original).]

In order to permit FDA to make a knowledgeable judgment about a new drug application, FDA regulations require applicants for new drug applications to provide FDA with a description and analysis of any data or information relevant to an evaluation of the safety and effectiveness of the drug product obtained or otherwise received by the applicant from any source, including information derived from clinical investigations. Applied Therapeutics, as the applicant of [**redacted**] failed to adhere to this requirement.

Specifically, according to Applied Therapeutics' October 19, 2023, Clinical Study Report for Protocol [**redacted**] which was submitted to FDA on December 28, 2023, the [**redacted**] was provided by [**redacted**] as a [**redacted**] mg/mL [**redacted**].

However, during FDA's inspection of Site [**redacted**] **FDA found that [redacted] had supplied the clinical sites for Protocol** [**redacted**] **with** [**redacted**] **mislabeled as** [**redacted**] **mg/mL, when in fact the amount of** [**redacted**] **supplied by** [**redacted**] **was** [**redacted**] **mg/mL. As a result of this error, between March and June 2021, clinical sites administered 80% of the protocol-required dose to subjects. Specifically, at least 19 subjects at Site**

[redacted] received a lower dosage of the [redacted] than the protocol required. On June 17, 2021, Applied Therapeutics notified clinical sites of this error, and on June 29, 2021, clinical sites were provided with a new formulation of the [redacted] at the correct concentration of [redacted] mg/mL. Clinical sites were also provided with an updated version of the pharmacy manual, with instructions on drug administration.

Applied Therapeutics failed to provide FDA with any description or analysis of the information describing the nature and extent of the dosing errors related to the mislabeled [redacted]. Specifically, Applied Therapeutics reported dose levels for subjects as stated in the protocol (for example, [redacted] mg/kg), rather than the actual dose levels administered. Information on the nature and extent of the dosing errors is relevant to an evaluation of the safety and effectiveness of the investigational drug product. Therefore, Applied Therapeutics failed to provide sufficient information at the time of submission of the application to enable FDA to make an informed decision regarding the impact of the dosing-error incident on study data. This failure raises significant concerns about the validity, reliability, and integrity of the data for Protocol [redacted]. Furthermore, Applied Therapeutics' failure to disclose this critical information raises significant concerns about the sponsor's oversight and conduct of clinical investigations, including its compliance with the reporting requirements for human drug products.

We acknowledge that this finding was not included on the Form FDA 483 you received, and therefore your written response does not address this finding.

We emphasize that as a sponsor, Applied Therapeutics has ultimate oversight of the clinical investigation, and was responsible for ensuring compliance with all applicable FDA regulations governing the conduct of clinical investigations. **Applied Therapeutics' failure to permit FDA access to verify records and reports related to a clinical investigation, and its failure to provide FDA information relevant to an evaluation of the safety and effectiveness of an [redacted] raise significant concerns about the validity and reliability of data collected for this clinical investigation**.

This letter is not intended to be an all-inclusive list of deficiencies with your clinical study of an [**redacted**]. As the sponsor, it is your responsibility to ensure adherence to each requirement of the law and relevant FDA regulations. You should address any deficiencies and establish procedures to ensure that any ongoing or future studies comply with FDA regulations.

This letter notifies you of our findings and provides you with an opportunity to address the above deficiencies. Within 15 business days of your receipt of this letter, you should notify this office in writing of the actions you have taken to prevent similar violations in the future. Failure to address this matter adequately may lead to regulatory action. If you believe that you have complied with the FD&C

> Act and relevant regulations, please include your reasoning and any supporting information for our consideration.
>
> Should you have any questions or concerns regarding this letter or the inspection, please email FDA at CDER-OSI-Communications@fda.hhs.gov. Your written response and any pertinent documentation should be addressed to: [names and addresses omitted].

291. In response to these disclosures, the price of Applied common stock fell $0.06 per share, or 3.4%, from a closing price on December 2, 2024 of $1.75 per share, to a closing price on December 3, 2024 of $1.69 per share, on above average volume of more than five times the average trading volume of Applied common stock from the start of the Class period through November 27, 2024.

292. On December 4, 2024, several news outlets reported on the FDA's findings, further disseminating the findings to the market. Fierce Biotech, a news service focused on biopharma, published an article titled "Applied Therapeutics' trial conduct scrutinized in FDA warning letter," noting that the FDA reprimanded the Company over deleted patient data and its mishandling of a serious dosing error.

> While Applied Therapeutics has vowed to reapply or appeal the FDA's recent rejection of its rare disease candidate govorestat, **deeper issues with the New York biotech's clinical trial conduct could put a damper on those plans. In a warning letter published Tuesday, the FDA scolded Applied on two counts related to its 47- patient study of govorestat in kids with classic galactosemia**.
>
> Specifically, **agency investigators took issue with electronic data deletion by a third-party vendor and the mishandling of a dosing error that led to some patients initially receiving lower levels of govorestat than intended**.
>
> The reprimand was issued around the same time the FDA rejected govorestat's approval bid in classic galactosemia, which causes developmental delays, speech problems and motor function abnormalities.
>
> A phase 3 trial of Applied's drug missed its primary endpoint in 2023—which isn't always a dealbreaker for rare disease approvals—but the company's clinical data package still fell short of the FDA's standards last week. The FDA's recent rejection sent Applied's share price tumbling some 80% in post-Thanksgiving trading.

Applied previously received a Form 483—a less severe FDA reprimand—around its trial conduct and responded to that write-up in May. That earlier wrist-slap did not include details on the dosing issue, the FDA explained in its warning letter.

Applied acknowledged the letter in a securities filing this week, noting that the regulator's complaints come down to "issues related to electronic data capture," which the biotech believes it addressed in prior communications, as well as a "dosing error in the dose escalation phase of the study" that the company said was "remedied prior to achieving maintenance dosing."

Applied said that it plans to respond to the FDA's warning letter within 15 business days.

Digging deeper into the FDA's concerns, the agency stated that two days after preannouncing an inspection of one of Applied's clinical trial sites in late April, a third-party vendor contracted by Applied deleted electronic data in a web-based data capturing platform.

In previous written correspondence with the FDA, Applied argued that the vendor deleted the data without consulting the company.

As for the dosing mishap, the FDA said that due to a labeling error, "clinical sites administered 80% of the protocol-required dose to subjects" between March and June of 2021. Applied alerted clinical sites about the error and provided a new formulation at the correct concentration in June of that same year, according to the warning letter.

Still, the FDA alleges that the company failed to provide the regulator with "any description or analysis of the information describing the nature and extent of the dosing errors."

In turn, the FDA says it lacked sufficient information at the time of Applied's approval submission to make an informed decision on the impact of the error on study data.

Govorestat, which is an aldose reductase inhibitor, has had something of a troubled history. Following the phase 3 miss last year, the FDA in March of this year delayed its decision deadline on the drug by three months, citing the need to further examine supplemental analyses of previously submitted data.

Regarding govorestat's fate in classic galactosemia, Applied has said it's reviewing feedback after the FDA's snub and plans to immediately request to meet with the regulator to "discuss requirements for a potential resubmission . . . or appeal of the decision."

The company has also maintained plans to file for approval of the drug in sorbitol dehydrogenase (SORD) deficiency in the first quarter of 2025. [(emphasis added).]

293. In response, the price of Applied common stock fell $0.31 per share, or 18.3%, from a closing price on December 3, 2024 of $1.69 per share, to a closing price on December 4, 2024 of $1.38 per share, on trading volume of 25.9 million shares, more than 13.6 times the average trading volume of Applied common stock from the start of the Class period through November 27, 2024.

294. On December 5, 2024, Stat News, a news service focused on medicine, health, and life sciences, published an article titled "Why Applied Therapeutics has a credibility problem:"

> **Applied Therapeutics' CEO Shoshana Shendelman has a debilitating credibility problem: She repeatedly misled investors prior to the Food and Drug Administration's rejection of the company's rare-disease drug.**
>
> **Throughout 2024, Shendelman assured investors that Applied's drug, called govorestat, was sailing through the FDA review process without major hitches. We now know she was lying by omission. The company was aware of significant problems with the govorestat application identified by the FDA, but Shendelman said nothing publicly.**
>
> **If members of the company's board have any sense of responsibility to shareholders, they'll take immediate steps to replace Shendelman. Allow her to resign or fire her, but either way, Applied Therapeutics needs a change in leadership if it's going to recover from this crisis.**
>
> On Nov. 27, Applied said the FDA rejected its application seeking approval of govorestat to treat children with galactosemia, a rare metabolic disease. The agency cited "deficiencies in the clinical application" as the reason for govorestat's rejection, according to Applied.
>
> Applied's stock price plunged 80%.
>
> **The FDA denial was obviously bad, but it was exacerbated by the disclosure on Tuesday of a warning letter sent by the FDA to Applied on Nov. 27.**
>
> **The warning letter cites Applied for drug-dosing errors in its clinical trial, and for deleting certain patient data from an electronic database that the agency sought to audit. The failures and deficiencies raised "significant concerns about the validity and reliability of data collected for this clinical investigation," the FDA concluded.**

Applied was made aware of the FDA's concerns in March, after an inspection conducted by the agency's review team in late April and early May, and in correspondence between the FDA and the company in September.

The timeline is particularly damning for Shendelman's shattered credibility. "Things are going very well with the FDA," Shendelman said in May during an onstage presentation at a health care investor conference.

In March, the FDA had extended the govorestat review by three months, but Shendelman brushed aside questions that this might signal a potential problem.

"We actually don't think that there are any major sticking points with the agency," she said, emphasizing that the FDA simply needed more time to review the application.

In August, Shendelman sold $4.7 million of Applied Therapeutics stock.

On Sept. 18, Applied announced that the FDA decided against convening an outside advisory committee to review the govorestat data.

Speaking at another health care investors conference on the same day, Shendelman said the FDA's decision, which came after a meeting with the company, was "very positive."

"Overall, our message there is that things are going well. We're very encouraged by the dialogue with the FDA, and we're excited about moving forward into this last stage of regulatory review," she added.

Applied's stock price soared, as investors interpreted the cancellation of the advisory committee meeting and Shendelman's comments as meaning the FDA was likely to approve the drug.

The opposite was actually true.

The FDA warning letter makes it clear that Shendelman was aware throughout 2024 that all was not well with the FDA's review. She decided to keep the critically important information to herself, while spinning a positive but misleading story to investors.

"The September 18 statement reflected Applied's optimism about the ongoing collaborative dialogue with the FDA during the NDA review process," Shendelman told me, in a statement sent through a company spokesperson. She declined an interview request.

"Applied remains committed to addressing the concerns outlined in the FDA warning letter swiftly and transparently," she added. [(emphasis added).]

295. In response, the price of Applied common stock fell $0.09 per share, or 6.5%, from a closing price on December 4, 2024 of $1.38 per share, to a closing price on December 5, 2024 of $1.29 per share, on above average volume of more than five times the average trading volume of Applied common stock from the start of the Class period through November 27, 2024.

296. Other research analysts found the disclosure of the Warning Letter and its contents to be significant. On December 20, 2024, during pre-market hours, RBC Capital Markets analyst Brian Abrahams issued a research note lowering the price target for Applied from $4.00 per share to $1.50 per share, and stating "[t]he content of the FDA's recent Warning Letter raises additional questions about data integrity and increases overall risk to the company's govorestat development path across indications.

3. Dr. Shendelman Resigns as CEO, President, Secretary, and Chair of Applied

297. On December 20, 2024, during pre-market hours, Applied issued a press release titled "Applied Therapeutics Appoints John H. Johnson as Executive Chairman" (the "12/20/2024 Press Release"), which announced that Dr. Shendelman had stepped down from her roles as President, CEO, Secretary, and Chair of the Board, and that Applied appointed John H. Johnson as Executive Chairman and Mr. Funtleyder as Interim CEO. These changes were accompanied by the withdrawal of the MAA for govorestat and a delay in the NDA submission for SORD Deficiency until after Q1 2025.

> John H. Johnson, a recognized leader in the pharmaceutical and biotechnology industry, has been named Executive Chairman;
>
> Dr. Shoshana Shendelman has stepped down as Chair and CEO; and
>
> Les Funtleyder, Applied Therapeutics' Chief Financial Officer, has been named Interim Chief Executive Officer.
>
> * * *

> Dr. Teena Lerner, Applied Therapeutics' Lead Independent Director, said, "On behalf of the Board, we strongly believe that John will be a tremendous addition to Applied Therapeutics. His experience leading pre-commercial businesses, deep knowledge of rare diseases and the commercialization process, along with his commitment to culture, are deeply aligned with Applied Therapeutics' priorities. We believe this change in leadership is the right next step for our Company, our shareholders and the patients we aim to serve."
>
> * * *
>
> As previously disclosed, in November 2024, the Company received a Complete Response Letter ("CRL") for the New Drug Application (NDA) for govorestat for the treatment of Classic Galactosemia. Given the leadership changes announced today, the Company continues to evaluate its response to the CRL, including any meeting request to discuss appropriate next steps with FDA.
>
> Following receipt of the CRL, the Company also today announced the withdrawal of the Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) for govorestat (AT-007) for the treatment of Classic Galactosemia, as more time is needed to acquire further data to support a European MAA.
>
> In light of recent regulatory developments, the Company will be closely examining the ongoing Sorbitol Dehydrogenase (SORD) Deficiency clinical development program and will continue to work with the FDA on the data needed to support an appropriate regulatory pathway for the drug, including ongoing work to provide the FDA with support for the potential use of the accelerated approval pathway for govorestat for the treatment of SORD Deficiency. To accommodate these ongoing workstreams, the Company currently expects to submit an NDA for govorestat for the treatment of SORD after the first quarter of 2025.

298. Also on December 20, 2024, during pre-market hours, the Company filed a Form 8-K with the SEC that discussed the resignation of Dr. Shendelman and the appointments of John Johnson and Mr. Funtleyder discussed in the 12/20/2024 Press Release (the "12/20/2024 Form 8-K"). The 12/20/2024 Form 8-K was signed by Mr. Funtleyder. Concerning Dr. Shendelman's resignation, the 12/20/2024 Form 8-K stated:

> On December 19, 2024, Dr. Shoshana Shendelman, a member of the Board and the Company's President, Chief Executive Officer and Secretary, stepped down from the role of President, Chief Executive Officer and Secretary and as a member of the Board. In connection with Dr. Shendelman's resignation, she entered into a Separation Agreement with the Company on December 19, 2024, and will be eligible to receive (i) the severance payments and benefits set forth in Section 9 of her Offer Letter, dated March 9, 2020, and attached as Exhibit 10.11 to the

> Company's Annual Report for the year ending December 31, 2023, with the cash payments made in a lump sum, and (ii) an additional lump sum cash amount equal to $2,100,000, in full satisfaction of her outstanding time- and performance-based restricted stock units.

299. In response, the price of Applied common stock fell $0.14 per share, or 13.7%, from a closing price of $1.02 per share on December 19, 2024 to a closing price of $0.88 per share on December 20, 2024, on above average volume of more than seven times the average trading volume of Applied common stock from the start of the Class period through November 27, 2024.

300. On April 28, 2025, Applied filed its Definitive Proxy for its 2025 Annual Meeting of Stockholders, and disclosed further information concerning Dr. Shendelman's severance package:

> Pursuant to the terms and conditions of the Shendelman Separation Agreement, Dr. Shendelman entered into a release of claims with the Company and in exchange she received (i) a lump sum cash severance amount equal to $997,500, (ii) an additional lump sum cash amount equal to $2,100,000, in full satisfaction of her outstanding RSUs and PSUs, (iii) continued payment by the Company of the cost of her (and her applicable dependents') health care coverage in effect as of her separation date under the Company's regular health plan or by paying her Consolidated Omnibus Reconciliation Act of 1985 (as amended, "COBRA") premiums for 12 months following her separation date or if earlier, until she obtains comparable health care coverage, and (iv) accelerated vesting of her Options that were unvested as of her separation date.

C. Additional Scienter Allegations

301. A host of facts, including and in addition to those discussed above, collectively support a strong inference that Defendants knew, or at minimum were extremely reckless in not knowing, the undisclosed facts as alleged herein and that their statements, as alleged herein, were materially false and misleading in violation of Section 10(b) and Rule 10b-5.

1. Class Period Stock Sales by Dr. Shendelman and Dr. Perfetti Enhance the Inference of Scienter and Motive

302. Dr. Shendelman profited massively from Applied's artificially inflated stock price during the Class Period by offloading her personally held Applied shares through a series of well-timed sales.

303. As alleged herein, during the Class Period, on March 14, 2024, June 10, 2024, and August 12 through 14, 2024, Dr. Shendelman sold 1,157,382 of her shares of Applied common stock for total proceeds of $6,696,111.64. These sales represented 14.32% of her holdings of 8,080,945 shares prior to the start of the Class Period, as reflected in a Schedule 13D/A filed by Dr. Shendelman with the SEC on November 13, 2023. The August 12 through 14, 2024 sales by themselves were for a total of 777,014 shares for total proceeds of $4,712,048.77.

304. Also, during the Class Period, Dr. Perfetti sold a total of 155,488 shares of Applied common stock for total proceeds of $824,516.75. On March 14, 2024, Dr. Perfetti sold 110,804 shares at an artificially inflated average sales price of $5.39 per share for total proceeds of $597,233.56. On June 6, 2024, Dr. Perfetti sold 22,003 shares at an artificially inflated average sales price of $4.32 per share for total proceeds of $95,052.96. On August 23, 2024, Dr. Perfetti sold 22,681 shares at an artificially inflated average sales price of $5.83 per share for total proceeds of $132,230.23. These stock sales represented 13.61% of Dr. Perfetti's holdings of 1,142,341 shares at the beginning of the Class Period, according to a March 14, 2024 Form 4 filed with the SEC.

305. These trades by Dr. Shendelman and Dr. Perfetti are sufficiently suspicious in timing and amount so as to preclude any affirmative defense that might otherwise have been available to their pre-planned sales made under any trading plans, and bolster an inference of scienter. All of the trades were made with knowledge of the Dosing Errors and that the NDA

omitted the Dosing Errors and the Dosing Errors Clinical Data. The trades on June 10, 2024 and August 12-14, 2024 were made after Dr. Shendelman received the Form 483 on May 3, 2024 and after Applied told the FDA on May 9, 2024 that Applied could not recover the deleted clinical data for 11 test subjects.

2. Dr. Shendelman Was Motivated to Have the NDA Approved and Keep the Stock Price High

306. In December 21, 2023, the Compensation Committee of the Applied Board awarded 2,200,000 restricted shares Applied common stock to Dr. Shendelman.

307. 1,100,000 of the restricted shares would vest in installments based on her continued employment over a four year period following the grant date.

308. The other 1,100,000 of the restricted shares would also vest based on her continued employment over a four year period following the grant date and the satisfaction of performance-based requirements relating to (a) achievement of a $6.00 stock price over a consecutive 20-day trading period and (b) the FDA approving the NDA and a potential new drug application for govorestat to treat Sorbitol Dehydrogenase.

309. From September 18, 2024 through October 15, 2024, the price of Applied common stock closed over $6.00 per share for 20 consecutive trading days, meeting one of two requirements for 1.1 million shares, or half, of Dr. Shendelman's December 2023 restricted stock award to be able to vest based on her continued employment. Withdrawing the NDA in light of the Dosing Errors or the Study Data Deletion would not only massively delay the second requirement of NDA approval, but would also cause the price of Applied's common stock to crater (as evidenced by the decline when the CRL and Warning Letter were revealed).

310. Notably, September 18, 2024 was the date that Applied issued a press release announcing a "regulatory update" and the cancellation of the Advisory Committee meeting for the

NDA that had previously been scheduled, and the date that Dr. Shendelman misleadingly characterized this as a positive development at 2024 Cantor Global Healthcare Conference, without disclosing the known significant negative factors impacting potential NDA approval of (a) the failure to include the Dosing Errors and Dosing Errors Clinical Data in the NDA and (b) the Study Data Deletion and that the FDA was unable to verify clinical data for 11 Pediatric Study patients due to the Study Data Deletion.

311. On September 18, 2024, the price of Applied common stock skyrocketed, increasing $3.20 per share, or 68.9%, from a closing price of $4.65 per share on September 17, 2024, to a closing price of $7.85 per share on September 18, 2024.

3. Dr. Shendelman and Dr. Perfetti were Key Employees and Authors of the Pediatric Study and Adult Study

312. As stated in the 2023 Form 10-K (at 71), Applied was "highly dependent on the services of" Dr. Shendelman and Dr. Perfetti**…** ***The loss of the services of either of these persons could impede the achievement of our research, development and commercialization objectives***."

313. In recognition of their importance, during the Class Period Dr. Shendelman and Dr. Perfetti were the two highest paid employees of Applied. In 2024, Dr. Shendelman's base salary was $665,000, and she was eligible to receive an annual performance and retention bonus of up to 50% of her annual base salary, which she did not receive in 2024. In 2023, Dr. Shendelman received a base salary of $630,000, a bonus of $315,000, stock awards worth $8,547,136, and other compensation of $1,077, for total compensation of $9,493,213.

314. In 2024 Dr. Perfetti's base salary was $580,000 and he was entitled to a discretionary bonus. In 2023, he received a salary of $550,000, a bonus of $300,000, stock awards worth $2,182,500, and other compensation of $10,761 for total compensation of $3,041,261.

315. Further, Dr. Shendelman and Dr. Perfetti were co-authors of the Pediatric Study, the results of which were submitted with the NDA without information on the Dosing Errors and Dosing Errors Clinical Data. The 11/6/2024 Pediatric Study Results specifically stated that Dr. Shendelman and Dr. Perfetti "designed and performed the stud[ies] and analyzed the data respectively" and "critically reviewed the manuscript and approved the final version for publication."

316. Because Dr. Shendelman and Dr. Perfetti were key employees of Applied, were authors and critically involved in Applied's "research, development and commercialization objectives," and were the authors and critically involved in the Pediatric Study, there is a strong inference that Dr. Shendelman and Dr. Perfetti were aware of, or were severely reckless in not being aware of, (a) the contents of the NDA and the Dosing Errors, (b) that Applied failed to provide FDA with any description or analysis of the information describing the nature and extent of the Dosing Errors in the NDA, and instead reported dose levels for subjects as stated in the protocol, rather than the actual dose levels administered, (c) that these omissions and errors in the NDA were, at a minimum severely reckless, and at worst a knowing violation of law, rules, and regulations, because information about the Dosing Errors and related clinical data was required to be included by the relevant FDA regulations, (d) that these omissions and errors in the NDA were a significant and material negative factor for approval of the NDA, and a serious risk that the FDA would reject NDA, and (e) that Defendants statements, as alleged herein, were materially false and misleading in violation of Section 10(b) and Rule 10b-5 as a result of the failure to disclose this information.

317. These facts also evidence a strong inference that Dr. Shendelman (who was given the Form 483) and Dr. Perfetti was aware of, or were severely reckless in not being aware of, (a)

the Form 483 and the Study Data Deletion, (b) that the Study Data Deletion and the inability of Applied to recover clinical data for 11 test subjects in the Pediatric Study was a violation of law, rules, and regulations, (c) that the Study Data Deletion was a major negative factor concerning the chances that the FDA would approve the NDA, and (d) that Defendants statements, as alleged herein, were materially false and misleading in violation of Section 10(b) and Rule 10b-5 as a result of the failure to disclose this information.

4. The Allegations of the Complaint Concern Core Operations of Applied - The Approval of the NDA and Subsequent Commercialization of Govorestat

318. During the Class Period, govorestat (AT-007) was Applied's lead drug candidate. Further, prior to and during the Class Period, Applied had never obtained regulatory approval for any drugs and had never commercialized any drugs.

319. During the Class Period, Applied's business and future prospects were dependent on its ability to option regulatory approval of and successfully commercialize its drug candidates.

320. During the Class Period, the NDA and the MAA were the first and only application for regulatory approval of drug candidate that Applied had filed. For example, during the Class Period, Dr. Shendelman and Applied repeatedly stated that "if approved, govorestat would be…the Company's first commercial product."

321. During the Class Period, after the NDA was submitted to the FDA, govorestat was the *only* product that had any path to generate revenue for the Company. As such, the Company's future prospects and business were highly dependent on the NDA being approved.

322. During the Class Period, Dr. Shendelman and Applied informed investors that they expected approval of the NDA, that they were preparing to commercialize govorestat upon that approval, and that if the NDA was approved, Applied could sell its "priority review voucher (PRV), [which] could substantially extend the Company's cash runway."

323. Also, according to the 2023 Form 10-K and Applied's Form 10-K for the fiscal year ended December 31, 2024, which was filed with the SEC on April 15, 2025 ("2024 Form 10-K"), during the Class Period, Applied had between 25 and 35 full time employees

324. Given the importance of govorestat's FDA approval to Applied's path to profitability, there is a strong inference that Defendants were aware of the Dosing Errors in the Pediatric Study at the times that the study was conducted, when they occurred, and when the NDA was submitted to the FDA. There is also a strong inference that Dr. Perfetti was made aware of the Data Deletion Issues after the Form 483 was submitted. The core nature of govorestat's FDA approval to Applied's financial sustainability strengthens the inference of scienter.

325. As such, the NDA and obtaining approval of the NDA were core operations of Applied, and this, combined with other facts evidencing scienter, including that Dr. Shendelman and Dr. Perfetti were key employees and authors of the Pediatric Study, evidence a strong inference that Dr. Shendelman and Dr. Perfetti were aware of, or were severely reckless in not being aware of, (a) the contents of the NDA and the Dosing Errors, (b) that Applied failed to provide FDA with any description or analysis of the information describing the nature and extent of the Dosing Errors in the NDA, and instead reported dose levels for subjects as stated in the protocol, rather than the actual dose levels administered, (c) that these omissions and errors in the NDA were, at a minimum severely reckless, and at worst a knowing violation of law, rules, and regulations, because information about the Dosing Errors and related clinical data was required to be included by the relevant FDA regulations, (d) that these omissions and errors in the NDA were a significant and material negative factor for approval of the NDA, and a serious risk that the FDA would reject NDA. and (e) that Defendants statements, as alleged herein, were materially false and misleading in violation of Section 10(b) and Rule 10b-5 as a result of the failure to disclose this information.

326. Further, the fact that the NDA and obtaining approval of the NDA were core operations of Applied, combined with other facts evidencing scienter, including that Dr. Shendelman and Dr. Perfetti were key employees and authors of the Pediatric Study, and the FDA's statement that Form 483's are shared with company senior management, evidence a strong inference that Dr. Shendelman (who was given the Form 483) and Dr. Perfetti was aware of, or were severely reckless in not being aware of, (a) the Form 483 and the Study Data Deletion, (b) that the Study Data Deletion and the inability of Applied to recover clinical data for 11 test subjects in the Pediatric Study was a violation of law, rules, and regulations, (c) that the Study Data Deletion was a major negative factor concerning the chances that the FDA would approve the NDA, and (d) that Defendants statements, as alleged herein, were materially false and misleading in violation of Section 10(b) and Rule 10b-5 as a result of the failure to disclose this information.

5. Defendants Spoke Regularly and in Detail About the Govorestat NDA, Thereby Putting Their Knowledge on the Subject at Issue

327. Throughout the Class Period, Defendants spoke regularly about govorestat, the NDA, the FDA's review of the NDA, communications with the FDA concerning the NDA, and plans for commercialization of govorestat. Indeed, Applied announced the govorestat NDA on the first day of the Class Period in the 1/3/2024 Press Release and 1/3/2024 Form 8-K, and made reference to it is most if not all subsequent SEC filings made during the Class Period.

328. By choosing to speak on these topics continuously throughout the Class Period, and revealing ***positive,*** or allegedly positive regulatory updates, Defendants put their knowledge on the subject at issue, and conveyed to investors that they knew that the NDA was complete with all required information and they were aware of no material negative information that would weigh against approval of the NDA. The alternative inference is that Defendants did not have any basis for discussing these topics, which does not negate or undercut scienter because it evinces an

extremely reckless disregard for the underlying facts that made Defendants' statements false or misleading during the Class Period.

6. Applied Acted with Corporate Scienter

329. The allegations above also establish a strong inference that Applied acted with corporate scienter throughout the Class Period, as its officers, management, and agents, including, but not limited to, Defendant Dr. Shendelman, Defendant Dr. Perfetti, and Dr. Bailey, had actual knowledge of the misrepresentations and omissions of material facts set forth herein (for which they had a duty to disclose), or acted with reckless disregard for the truth because they failed to ascertain and to disclose such facts, even though such facts were available to them.

330. The scienter of the Individual Defendants and other employees and agents of the Company is similarly imputed to Applied under *respondeat superior* and agency principles.

331. Corporate scienter is supported by the fact that Applied was a small company, with just 25 full time employees at the start of the Class Period, wherein the Individual Defendants were directly involved in the NDA and the clinical trials that were included in the NDA.

332. The scienter of Applied is also evidenced by the knowledge of Dr. Bailey, who was another co-author of, designed, and reviewed the data concerning, the Pediatric Study. Dr. Bailey was also an author of and part of the 9/4/2024 Presentation.

D. Loss Causation

333. As detailed herein, throughout the Class Period, the Defendants made materially false and misleading statements that artificially inflated the price of Applied common stock.

334. When the truth about the Defendants' prior misrepresentations was disclosed and became apparent to the market, the prices of Applied common stock declined significantly as the prior, artificial inflation came out of the prices of the securities.

335. By not publicly disclosing the adverse facts detailed herein, the Defendants presented a misleading picture of the Company's business, prospects, and operations.

336. The Defendants' false and misleading statements caused Applied common stock to trade at artificially inflated levels throughout the Class Period.

337. The artificial inflation of Applied's common stock price was removed beginning on November 27, 2024, during post-market hours, when Applied announced that the FDA had issued the CLR denying govorestat's approval. Applied announced that the "CRL indicates that the FDA completed its review of the application and determined that it is unable to approve the NDA in its current form, citing deficiencies in the clinical application."

338. However, Applied continued to reassure investors that govorestat's approval was imminent. For example, in the announcement, Dr. Shendelman, stated that "As we move forward, we plan to work with the FDA to address the concerns in the CRL and determine an expeditious path to bring this much needed treatment to patients." Notably, Applied continued to conceal the revelations of the Warning Letter, which was sent to by the FDA to Dr. Shendelman by email on November 27, 2024.

339. The market was stunned, and analysts reacted in immediate and uniform shock to the disclosure of the CRL, as outlined in paragraphs278-282. For example, the next day, William Blair characterized the CRL as "a Major Setback" and that following: "[a]fter speaking with management, it noted that the FDA had not provided enough information on the reason for the CRL, but suspects it was related to the efficacy package as opposed to CMC or safety." Leerink Partners expressed shock, and noted that the CRL "comes as a major surprise, given the progress the company appeared to be making with the FDA" and "[w]e thought the FDA review had been progressing favorably based on the information available to us." Similarly, RBC Capital Markets

issued a report that "[t]he CRL for govorestat in galactosemia is disappointing, and we believe creates significant uncertainties around a future path forward for the drug in that indication."

340. In direct response to this partial corrective disclosure, the price of Applied common stock collapsed by $6.54 per share, from a closing price of $8.57 on Wednesday, November 27, 2024 to $2.03 per share on the next day of trading on Friday, November 29, 2024. This amounted to a drop in stock price of 76.3%, on extremely high volume of more than 23 times the average trading volume of Applied common stock from the start of the Class Period through November 27, 2024. The price of Applied Therapeutics common stock continued its decline in response to the disclosure of the CRL and rejection of the NDA on Monday December 2, 2024, closing at $1.75 per share, an additional decline of $0.28 per share on volume nearly 16 times the average trading volume of Applied common stock from the start of the Class Period through November 27, 2024. .

341. Thus, the market understood the announcement of the CRL and that the NDA had not been approved to a partial corrective disclosure of the Defendants prior class period misstatements that misrepresented, *inter alia*, that (a) the NDA was complete and contained all required information, (b) they were aware of no negative factors, new information, or regulatory updates that could lead the FDA to reject the NDA, (c) things were "going very well" with the FDA, and (d) there was reasonable basis to expect approval of the NDA in the "near term."

342. On December 2, 2024, during post-market hours, Applied filed a Form 8-K with the SEC that announced it had received the Warning Letter. The following day, on December 3, 2024, the FDA posted a copy of the Warning Letter on its website, which Applied had received on November 27, 2024 and failed to disclose in its November 27, 2024 announcements of the CRL and that the NDA had not been approved.

343. The Warning Letter finally revealed the full extent of the problems plaguing the govorestat NDA, including the Dosing Errors and the Study Data Deletion, which was personally discussed with Shendelman on May 3, 2024, and which "raise[d] significant concerns about the validity and reliability of data collected for this clinical investigation."

344. In direct response to these partial corrective disclosures, the price of Applied common stock fell $0.06 per share, or 3.4%, from a closing price on December 2, 2024 of $1.75 per share, to a closing price on December 3, 2024 of $1.69 per share, on above average volume of more than five times the average trading volume of Applied common stock from the start of the Class period through November 27, 2024.

345. The revelations of the Warning Letter left investors, still reeling from the November 27 disclosure, aghast. On December 4, 2024, several news outlets reported on the FDA's findings, further disseminating the findings to the market. Fierce Biotech published an article titled "Applied Therapeutics' trial conduct scrutinized in FDA warning letter," noting that the FDA reprimanded the Company over deleted patient data and its mishandling of a serious dosing error.

346. In direct response to these partial corrective disclosures, the price of Applied common stock fell $0.31 per share, or 18.3%, from a closing price on December 3, 2024 of $1.69 per share, to a closing price on December 4, 2024 of $1.38 per share, on above average volume of more than 13.6 times the average trading volume of Applied common stock from the start of the Class period through November 27, 2024.

347. A December 5, 2024 article from Stat News decried the Company and Dr. Shendelman's credibility, and stated that she "repeatedly misled investors prior to the Food and Drug Administration's rejection of the company's rare-disease drug. Throughout 2024, Dr. Shendelman assured investors that Applied's drug, called govorestat, was sailing through the FDA

review process without major hitches. We now know she was lying by omission. The company was aware of significant problems with the govorestat application identified by the FDA, but Dr. Shendelman said nothing publicly."

348. In direct response to these disclosures, the price of Applied common stock fell $0.09 per share, or 6.5%, from a closing price on December 4, 2024 of $1.38 per share, to a closing price on December 5, 2024 of $1.29 per share, on above average volume of more than five times the average trading volume of Applied common stock from the start of the Class period through November 27, 2024.

349. In total, in response to the December 2, 3, 4, and 5 partial corrective disclosures, Applied common stock fell $0.46 per share, or 26.3%, from a closing price of $1.75 per share on December 2, 2024, to a closing price of $1.29 per share on December 5, 2024.

350. Thus, as demonstrated above, the market understood the Warning Letter to be a partial corrective disclosure of the Defendants prior class period misstatements that misrepresented, *inter alia*, that (a) the NDA was complete and contained all required information, (b) communications with the FDA were "normal course," (c) things were "going very well" with the FDA, and (d) there was reasonable basis to expect approval of the NDA in the "near term," and (e) there were known no negative factors, new information, risks, or regulatory updates, such as Dosing Errors, the Form 483, and the Study Data Deletion, that could lead the FDA to reject the NDA.

351. Finally, on December 20, 2024, during pre-market hours, Applied issued a press release announcing that Shendelman had resigned from her positions as CEO, Chair, Secretary, and President on December 19, 2024.

352. In direct response to these disclosures, the price of Applied common stock fell $0.14 per share, or 13.7%, from a closing price of $1.02 per share on December 19, 2024 to a closing price of $0.88 per share on December 20, 2024, on above average volume of more than seven times the average trading volume of Applied common stock from the start of the Class period through November 27, 2024.

353. A report issued by RBC Capital Markets on December 20, 2024 after Dr. Dr. Shendelman was forced to resign stated bluntly that "[t]he content of the FDA's recent Warning Letter raises additional questions about data integrity and increases overall risk to the company's govorestat development path across indications[.]"

354. Thus, the market understood that Dr. Shendelman's resignation to be a further partial corrective disclosure of the Defendants prior class period misstatements.

355. By not disclosing the adverse facts detailed herein, the Defendants presented a misleading picture of Applied's business, risks, and current and future financial prospects. When the truth about the Company was revealed to the market, the prices of Applied common stock fell significantly, as detailed above, removing the inflation from the Defendants' misrepresentations and causing economic loss to investors who had purchased Applied common stock during the Class Period.

356. The decline in the prices of Applied common stock after the corrective disclosures came to light was a direct result of the nature and extent of the Defendants' misrepresentations being revealed to investors and the market. The timing and magnitude of the price declines in Applied securities negates any inference that the losses suffered by Plaintiff and the other members of the Class were caused by changed market conditions, macroeconomic or market trends, industry factors or conditions, or unrelated Company-specific facts unrelated to the Defendants' material

misrepresentations. Rather, the substantial decline in Applied's stock was a foreseeable and direct result of the revelation of previously undisclosed facts, facts that had been intentionally or recklessly withheld by Defendants during the Class Period.

357. Plaintiff and the other Class members purchased shares of Applied common stock at prices that were inflated by Defendants' false and misleading statements. The economic loss, *i.e.*, damages, suffered by Plaintiff and the other members of Class was a direct result of the Defendants' false statements that artificially inflated the price of Applied common stock and the subsequent significant declines in the value of Applied common stock when the Defendants' prior misrepresentations were disclosed.

358. During the Class Period, as detailed herein, the Defendants made materially false and misleading statements that artificially inflated the prices of Applied common stock by failing to disclose and misrepresenting the adverse facts detailed herein. When the Defendants' prior misrepresentations and fraudulent conduct were disclosed and became apparent to the market, the prices of Applied common stock securities declined significantly as the prior artificial inflation came out of the stock's price. Accordingly, the economic harm suffered by investors was a direct consequence of Defendants' wrongful conduct and the subsequent correction of the market's understanding of the Company's true condition.

E. Applicability of the Presumption of Reliance and the Fraud-On-The-Market Doctrine

359. Applied's common stock traded in an open, well-developed, and efficient market at all relevant times.

360. As a result of the materially false and/or misleading statements particularized in this Complaint, Applied common stock traded at artificially inflated and/or maintained prices during the Class Period. Lead Plaintiff and other members of the Class purchased the Company's

common stock relying upon the integrity of the market price of Applied common stock and market information relating to Applied and have been damaged thereby.

361. At all times relevant, the market for Applied common stock was an efficient market for the following reasons, among others:

a) Applied common stock was listed and actively traded on the NASDAQ, a highly efficient and automated market;

b) Applied filed periodic public reports with the SEC and/or the NASDAQ;

c) Applied regularly communicated with public investors via established market communication mechanisms, including through regular dissemination of press releases on major newswire services, participating in investor and industry conferences, and through other wide-ranging public disclosures, such as communications with the financial press and other similar reporting services; and/or

d) Applied was followed by securities analysts employed by brokerage firms, including RBC Capital Markets, Leerink Partners, Baird, William Blair, Citigroup, and UBS Securities, who wrote reports about the Company. Each of these reports was publicly available and entered the public marketplace.

362. As a result of the foregoing, the market for Applied common stock promptly digested current information regarding Applied from all publicly available sources and reflected such information in the prices of the securities. Under these circumstances, all purchasers of Applied common stock during the Class Period suffered similar injury through their purchase of Applied common stock at artificially inflated and/or maintained prices, and a presumption of reliance applies.

363. Therefore, Lead Plaintiff and the Class are entitled to a presumption of reliance pursuant to *Basic Inc. v. Levinson*, 485 U.S. 224 (1988).

364. A Class-wide presumption of reliance is also appropriate in this action under the Supreme Court's holding in *Affiliated Ute Citizens of Utah v. United States*, 406 U.S. 128 (1972), because the Classes' claims are, in large part, grounded in the Defendants' omissions of material facts necessary to make the statements made by the Defendants not misleading.

365. Because this action involves the Defendants' failure to disclose material adverse information regarding the Company's business, operations, and prospects - information that the Defendants were obligated to disclose during the Class Period but did not - positive proof of reliance is not a prerequisite to recovery. All that is necessary is that the facts withheld be material in the sense that a reasonable investor might have considered them important in the making of investment decisions. Given the importance of the Class Period material misstatements and omissions set forth above, that requirement is satisfied here.

F. Inapplicability of the Statutory Safe Harbor

366. Defendants cannot rely on the statutory safe harbor for forward-looking statements under the Private Securities Litigation Reform Act of 1995. The alleged misrepresentations and half-truths concern present or historical facts or conditions, such as the results and conduct of clinical trials, regulatory interactions concerning the NDA, and the content of submissions to the FDA, including the NDA, and not future expectations. These statements involved material misstatements or failures to disclose adverse information that had already occurred at the time the statements were made.

367. In addition, to the extent certain of the statements alleged to be materially false and misleading in violation of Section 10(b) or Rule 10b-5 may be characterized as forward-looking, they were not identified as "forward-looking statements" when made, and there were no

meaningful cautionary statements identifying important factors that could cause actual results to differ materially from those in the purportedly forward-looking statements.

368. Further, to the extent that any statements alleged to be materially false and misleading in violation of Section 10(b) or Rule 10b-5 may be characterized as forward-looking, the Defendants are liable for those forward looking statements because the speaker had actual knowledge that the forward-looking statement was materially false and misleading, and/or the statement was authorized by an officer of Applied who knew the statement was false and misleading. Dr. Shendelman and Dr. Perfetti were the author of, or authorized, all the statements alleged to be false and misleading herein. They had actual knowledge of the Dosing Errors, that information about and clinical data concerning the Dosing Errors was not included in the NDA, the Study Data Deletion and the Form 483, and that these were material negative factors that reduced the chance that the FDA would approve the NDA.

CLASS ACTION ALLEGATIONS

369. Plaintiff brings this action as a class action pursuant to Federal Rule of Civil Procedure 23(a) and 23(b)(3) on behalf of a Class consisting of all persons that purchased or otherwise acquired the publicly traded common stock of Applied on a U.S. based exchange during the Class Period.

370. Excluded from the Class are the Defendants; the current and former officers, directors, and employees of Applied (the "Excluded Persons"); any person or entity that purchased Applied securities in the 3/1/2024 Private Placement (the "Private Placement Investors"); members of Defendants', Excluded Persons', or Private Placement Investors' immediate families, legal representatives, heirs, successors or assigns; and any entity in which Defendants, the Excluded Persons, or the Private Placement Investors have or had a controlling interest.

371. The members of the Class are so numerous that joinder of all members is impracticable. As of November 8, 2023, shortly before the start of the Class Period, Applied had 77,229,207 shares of common stock outstanding. As of November 6, 2024, near the end of the Class Period, Applied had 116,356,474 shares of common stock outstanding. The Company's common stock actively traded on the NASDAQ under the symbol "APLT."

372. While the exact number of the members of the Class is unknown to Lead Plaintiff at this time and can only be ascertained through appropriate discovery, Lead Plaintiff believes that there are at least hundreds, if not thousands, of members in the proposed Class. Record owners and other members of the Class may be identified from records maintained by Applied or its transfer agent and may be notified of the pendency of this action by mail, using the form of notice similar to that customarily used in securities class actions.

373. Plaintiff's claims are typical of the claims of the members of the Class as all members of the Class are similarly affected by Defendants' wrongful conduct in violation of the Exchange Act complained of herein.

374. Plaintiff will fairly and adequately protect the interests of the members of the Class and has retained counsel competent and experienced in class and securities litigation.

375. Common questions of law and fact exist among all members of the Class and predominate over any questions affecting individual members. Among the questions of law or fact common to the Class and its claims for violations of the Exchange Act are:

a) whether the Defendants violated Section 10(b) of the Exchange Act and/or Rule 10b-5 promulgated thereunder;

b) whether statements made by the Defendants to the investing public in SEC filings, press releases, investor presentations, industry conferences, and other public

statements identified herein were or contained untrue statements of material fact or omitted to state material facts necessary to make the statements made not misleading;

c) whether the Defendants acted with scienter when making materially false or materially misleading statements;

d) Whether the prices of Applied common stock during the Class Period was artificially inflated because of the Defendants' conduct complained of herein;

e) whether the Individual Defendants were control persons of Applied for purposes of Section 20(a) of the Exchange Act; and

f) to what extent members of the Class have sustained damages, and if so, the proper measure of damages.

376. A class action is superior to all other available methods for the fair and efficient adjudication of this controversy since joinder of all members is impracticable. Furthermore, since the damages suffered by individual Class members may be relatively small, the expense and burden of individual litigation makes it impossible for members of the Classes to individually redress the wrongs done to them. There will be no difficulty in the management of this action as a class action.

CAUSES OF ACTION

COUNT I
Violations of Section 10(b) of the Securities Act and Rule 10b-5 Promulgated Thereunder Against All Defendants

377. Plaintiff repeats and realleges each and every allegation contained above as if fully set forth herein.

378. This Count is asserted on behalf of Plaintiff and the Class against all Defendants pursuant to Section 10(b) of the Exchange Act, 15 U.S.C. §78j(b), and Rule 10b-5 promulgated thereunder by the SEC, 17 C.F.R. § 240.10b-5.

379. Section 10(b) of the Exchange Act provides that:

> It shall be unlawful for any person, directly or indirectly, by the use of any means or instrumentality of interstate commerce or of the mails, or of any facility of any national securities exchange… To use or employ, in connection with the purchase or sale of any security registered on a national securities exchange or any security not so registered, or any securities-based swap agreement any manipulative or deceptive device or contrivance in contravention of such rules and regulations as the Commission may prescribe as necessary or appropriate in the public interest or for the protection of investors.

380. Rule 10b-5 provides that:

> It shall be unlawful for any person, directly or indirectly, by the use of any means or instrumentality of interstate commerce, or of the mails or of any facility of any national securities exchange,
>
> (a) To employ any device, scheme, or artifice to defraud,
>
> (b) To make any untrue statement of a material fact or to omit to state a material fact necessary in order to make the statements made, in the light of the circumstances under which they were made, not misleading, or
>
> (c) To engage in any act, practice, or course of business which operates or would operate as a fraud or deceit upon any person,
>
> in connection with the purchase or sale of any security.

381. Throughout the Class Period, the Defendants, individually and in concert, directly or indirectly disseminated or approved the false statements specified above, which they knew or deliberately disregarded were false or misleading in that they contained untrue statements of material fact or failed to disclose material facts necessary to make the statements made, in light of the circumstances under which they were made, not misleading.

382. During the Class Period, the Defendants carried out a plan, scheme, and course of conduct that was intended to and, throughout the Class Period, did: (i) deceive the investing public, including Plaintiff and other Class members, as alleged herein; (ii) artificially inflate and maintain the market price of Applied common stock; and (iii) caused Plaintiff and other members of the Class, in ignorance of the falsity of the Defendants' statements, to purchase or otherwise acquire

Applied common stock at artificially inflated prices. In furtherance of this unlawful scheme, plan, and course of conduct, the Defendants took the actions set forth herein.

383. The Individual Defendants (a) Directly participated in the management of Applied; (b) were directly involved in the day-to-day operations of Applied at the highest levels; (c) were privy to confidential proprietary information concerning Applied and its business and operations; (d) were directly or indirectly involved in the oversight or implementation of Applied's internal controls; and/or (e) were directly or indirectly involved in drafting, producing, reviewing and/or disseminating the untrue statements of a material fact or statements that omitted to state material facts required to be stated or necessary to make the statements made not misleading; were aware of or recklessly disregarded the fact that the false and misleading statements were being issued concerning Applied; and/or approved or ratified these statements in violation of the federal securities laws.

384. The Individual Defendants, who are or were the senior officers and/or directors of the Company, had actual knowledge of the material omissions and/or the falsity of the material statements set forth above, and intended to deceive Plaintiff and the other members of the Class, or, in the alternative, acted with reckless disregard for the truth when they failed to ascertain and disclose the true facts in the statements made by them or other Applied personnel to members of the investing public, including Plaintiff and the Class.

385. As set forth herein, the Defendants acted with scienter in that they knew that the public documents and statements issued or disseminated in the name of Applied were materially false or misleading; knew that such statements or documents would be issued or disseminated to the investing public; and knowingly and substantially participated, or acquiesced in the issuance or dissemination of such statements or documents as primary violations of the securities laws.

These Defendants by virtue of their receipt of information reflecting the true facts of Applied, their control over, and/or receipt and/or modification of Applied's allegedly materially misleading statements, and/or their associations with the Company which made them privy to confidential proprietary information concerning Applied, participated in the fraudulent scheme alleged herein.

386. As a result of Defendants' misconduct, the market price of Applied common stock was artificially inflated throughout the Class Period. Plaintiff and other Class members relied, either directly or indirectly, on the false and misleading statements disseminated by Defendants, and/or relied upon the integrity of the market in purchasing their securities. Plaintiff and the Class would not have purchased or otherwise acquired Applied securities at the prices they paid, or at all, had they known the truth.

387. When the truth was ultimately disclosed, including the issuance of the FDA's Complete Response Letter, the publication of the FDA's Warning Letter outlining the Company's regulatory failures, and revelations that Defendants had withheld critical information from investors, the price of Applied common stock declined precipitously, causing substantial losses and damages to Plaintiff and the Class.

388. As a result of the wrongful conduct alleged herein, Plaintiff and other members of the Class have suffered damages in an amount to be established at trial.

389. By reason of the foregoing, the Defendants are liable to the Plaintiff and the other members of the Class for substantial damages that the Plaintiff and the Class have suffered in connection with their respective purchases or acquisitions of Applied common stock during the Class Period.

COUNT II
Violations of Section 20(a) of the Securities Act
Against Defendants Shoshana Shendelman and Ricardo Perfetti

390. Plaintiff repeats and realleges each and every allegation contained in the foregoing paragraphs as if fully set forth herein.

391. This Count is asserted on behalf of Plaintiff and the Class against the Individual Defendants pursuant to Section 20(a) of the Exchange Act, 15 U.S.C. §78t(a).

392. Section 20(a) of the Exchange Act provides that:

> Every person who, directly or indirectly, controls any person liable under any provision of this chapter or of any rule or regulation thereunder shall also be liable jointly and severally with and to the same extent as such controlled person to any person to whom such controlled person is liable (including to the Commission in any action brought under paragraph (1) or (3) of section 78u(d) of this title), unless the controlling person acted in good faith and did not directly or indirectly induce the act or acts constituting the violation or cause of action.

393. As alleged above, the Applied violated Section 10(b) of the Exchange Act and/or SEC Rule 10b-5 promulgated thereunder.

394. Throughout the Class Period, each of the Individual Defendants served in senior executive roles at Applied, Dr. Shendelman as CEO, President, Secretary, Chair of the Board, and Dr. Perfetti as CMO.

395. During the Class Period, the Individual Defendants were privy to non-public information concerning the Company, its business and operations, the Company's NDA, the Dosing Errors that affected key clinical data, the deletion of eCOA records, and the significant regulatory concerns raised by the FDA, via access to internal corporate documents, conversations and connections with other corporate officers and employees, attendance at management and Board meetings and committees thereof and via reports and other information provided to them in connection therewith. Because of their possession of such information, the Individual Defendants knew or recklessly disregarded the fact that adverse facts specified herein had not been disclosed

to, and were being concealed from, the investing public. Plaintiff and other members of the Class had no access to such information, which was, and remains, solely under the control of the Defendants.

396. The Individual Defendants were involved in drafting, producing, reviewing and/or disseminating the materially false and misleading statements complained of herein. The Defendants were aware (or recklessly disregarded) that materially false and misleading statements were being issued by the Company and nevertheless approved, ratified and/or failed to correct those statements, in violation of federal securities laws. Throughout the Class Period, the Individual Defendants were able to, and did, control the contents of the Company's SEC filings, reports, press releases, and other public statements. The Individual Defendants were provided with copies of, reviewed and approved, and/or signed such filings, reports, releases and other statements prior to or shortly after their issuance and had the ability or opportunity to prevent their issuance or to cause them to be corrected.

397. By virtue of their positions, both exercised control over the operations, strategic direction, and public disclosures of the Company. As officers of a publicly traded company, the Individual Defendants had a duty to disseminate accurate and truthful information and to correct any materially false or misleading information that had been disseminated. The Individual Defendants also were able to, and did, directly or indirectly, control the conduct of Applied's business, the information contained in its filings with the SEC, and its public statements. Moreover, the Individual Defendants made or directed the making of affirmative statements to securities analysts and the investing public at large, and participated in meetings and discussions concerning such statements. Because of their positions and access to material non-public information available to them but not the public, the Individual Defendants knew that the adverse

facts specified herein had not been disclosed to and were being concealed from the public and that the positive representations that were being made were false and misleading. As a result, the Individual Defendants are responsible for the accuracy of Applied's corporate statements detailed herein and are therefore responsible and liable for the misrepresentations contained herein.

398. Because of their high-ranking positions and roles in shaping the Company's regulatory and investor communications, the Individual Defendants were and acted as "controlling persons" of Applied within the meaning of Section 20(a) of the Exchange Act. Each had the power to influence and control, and did influence and control, directly or indirectly, the decision-making processes of the Company, including the content and issuance of the false and misleading statements alleged herein. Each had the power and authority to cause Applied to engage in the wrongful conduct complained of herein. The Individual Defendants controlled Applied and all of its employees.

399. As alleged above, Applied is a primary violator of Section 10(b) of the Exchange Act and SEC Rule 10b-5. By reason of their conduct, the Individual Defendants are jointly and severally liable to Plaintiff and the Class for the damages they suffered as a result of the Company's violations of federal securities laws.

400. As a direct and proximate result of the wrongful conduct of Applied and the Individual Defendants, Plaintiff and members of the Class suffered damages in connection with their respective purchases and acquisitions of the Company's securities during the Class Period.

401. By reason of the misconduct alleged herein, and pursuant to Section 20(a) of the Exchange Act, the Individual Defendants are liable to Plaintiff and the Class for the violations of Section 10(b) committed by the Company.

PRAYER FOR RELIEF

WHEREFORE, Plaintiff respectfully requests that the Court enter judgment in favor of Plaintiff and the Class and against Defendants as follows:

A. Certifying this action as a class action pursuant to Rule 23 of the Federal Rules of Civil Procedure, appointing Lead Plaintiff as the Class Representative, and designating Lead Counsel as Class Counsel.

B. Awarding compensatory damages in favor of Plaintiff and the Class for all losses sustained as a result of Defendants' wrongdoing, in an amount to be proven at trial, together with pre-judgment and post-judgment interest as allowed by law;

C. Awarding Plaintiff and the Class their reasonable costs and expenses incurred in this action, including attorneys' and experts' fees; and

D. Awarding such other and further relief as the Court may deem just and proper.

JURY DEMAND

Plaintiff hereby demands a trial by jury.

Dated: May 2, 2025
New York, NY

Respectfully submitted,

WOLF POPPER LLP

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